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Burnout Syndrome among Saudi Medical Residents: A Controlled Study

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Abstract:

To investigate resident burnout among different medical specialties. Method: Maslach Burnout Inventory forms had been fulfilled by 71 residents from eight different medical specialties. All residents were from Saudi Board Program. Results: A greater percentage of senior residents (34%) were doing recreational activities than junior residents (28%). Eighty percent of residents were not satisfied with the number of working hours. There was no significant difference between junior and senior residents regarding to the number of calls per week. There was no significant difference between junior and senior residents regarding to the three mean values of the subscales of MBI (t-values = -0.8, -0.9, -1.5 and significance = 0.5, 0.4, 0.1). Medical residents had a significant lower mean values regarding to accomplishment subscale (35±10) than the other 4 main sections of residents (f = 2.2, p = 0.04). Surgical residents got significantly higher mean scores in two items of MBI than medical residents. These two items are sense of fatigue and dealing with their patients as objects. The test which had been used was t-test (t = 2.4 and 3.5) respectively, significances were 0.02 and 0.001 Conclusions: Junior Medical residents are the least who suffer from burnout, followed by senior medical residents. Obstetrics, Gynecology and Surgical residents are the most sufferer from burnout symptoms among all specialties included in this study. Numbers of working hours, number of on calls per week, and residents who live away from their places of work are issues need to be discussed with the decision makers.

Introduction:

Maslach defined burnout syndrome as a loss of interest and care for users and consequently the development of a relationship characterized by detachment and coldness within an environmental model including situational factors like social and environmental context and the nature of the job (Maslach C, et al 2001). Maslach distinguishing three components of burnout: emotional depletion, indifferent attitudes to colleagues and users, and negative self-evaluation of job performance (Thomas NK, 2004).

The 80 hours-per-week limits implemented nationally on residents' work have been sought, in part, as a response to resident burnout, which has been linked to decreased job performance (Lemkau J, et al 1994) (i.e., increased medical errors), low career satisfaction, and a decrease in empathic concern, including feeling less humanistic (Nyssen AS, et al 2003). Using the Maslach Burnout Inventory (MBI) (Maslach C, et al 1996), a validated and reliable tool, one survey of an internal medicine residency program found that 76% of the respondents met criteria for burnout (Iacovides A, et al 2003). Two years after New York State implemented revisions to the state health code (section 405), which required reduction in on-call work and increased supervision, residents reported diminished fatigue and better patient care (Geurts S, et al 1999). Home-related Stressors for residents may also play

a vital role in work-related fatigue (Levey RE, 2001).

Burnout differs from depression, in that it is confined to the workplace. However, if generalization to the home environment occurs, burnout may progress to clinical depression, although such a temporal relationship is not well established(Levine RE, et al 2003, Veasey S, et al 2002, Beckman JA & Fang JC, 2002).

Based on these results, we undertook checking a sample of residents to measure their burnout and explore the association with specialty, the effects of recreational activities, their frequencies, satisfaction with working hours, number of calls per week, the distance of residents

Housing from the working place, stager in training e.g. junior or senior, and which specialties are more vulnerable to burnout syndrome?.

Subjects and methods:

Subjects of this study are all residents working at King Abdul-Aziz Medical City (KAMC) during March 2005. Confounding variables were assessed among all residents e.g. age, sex, marital status, recreational activities, their frequencies, distance of their living away from KAMC, number of on calls & working hours.

There were 71 residents, who were distributed as the following:

Three residents from ENT, Two residents from ophthalmology, One resident from ER, Ten residents from General Surgery, Ten residents from Obstetrics and Gynecology, Nine residents from Radiology, Seventeen residents from pediatrics, Nineteen residents from Medicine

MBI was used as a measure to assess the quantity of burnout among all residents (who are under the supervision of Saudi Board Program) and working at KAMC. Given the stress that accompanies this kind of uncertain job situation when hospitals are undergoing restructuring, nurses are particularly prone to developing psychological burnout. Maslach burnout Inventory consists of three different aspects: emotional exhaustion, depersonalization, and reduced personal accomplishment. Emotional exhaustion is defined as feelings of being emotionally overextended and drained by others. Depersonalization is a callous response toward people who are the recipients of one's services. Lack of personal accomplishment is a decline in one's feelings of competence and successful achievement in one's work with people. Burnout is considered a special type of prolonged exposure to occupational stress and results from interpersonal demands at work (Maslach C, et al 1996)

MBI consists of 22 statements representing 3 main components:

A-Emotional exhaustion are represented by statements. Their numbers are: 4,5,7,9,10,11,12,15,17,18,19,21,22

B-Depersonalization are represented by statements. Their numbers are: 1,2,3,4,6,7,8,9,12,13,14,16,17,18,19,20,21

C-Accomplishment are represented by statements. Their numbers are :1,2,3,5,6,8,10,11,13,14,15,16,20,22

Statistical Analysis:

All analyses were conducted with SPSS software. Means, standard deviations (SD) and Qui square are reported. Comparisons between two quantitative means'

differences were assessed using the two-sample t- test and between more than two means were assessed using f-test (ANOVA). Significance was set post-hoc at 0.05 (SPSS version 10.1, 2001).

Results:

MBI forms were distributed among 79 Arab Board program residents at King Abdul-Aziz Medical City. Seventy one of them completed the answers of MBI forms, while 8 residents were too busy to fulfill these forms. The 2nd, 3rd, and 4th authors, who were well oriented by the items of MBI, helped the other residents in fulfilling the forms of MBI. The forms of MBI included some other data like: age, sex, marital status, doing recreational activities, and the frequency of doing these activities, the satisfaction with the number of working hours, the distance of housing from the hospital, and the number of calls per week.

There was no significant difference between junior and senior residents as regards to gender (x2 = 0.13 and significance is = 0.8) (Table 1).

Table (1):: Sex distribution among junior and senior residents

	Male	%	Female	%	Total	%	X2	Significance
Junior Residents	24	33.8%	15	21.1%	39	54.9%	0.13	0.8
Senior Residents	21	29.6%	11	15.5%	32	45.1%		
Total	45	63.4%	26	36.6%	71	100		

Level of significance at $p < 0.05$

Most of the residents in our study were married. There were 17 single junior residents, 9 single senior residents, and one divorced resident. The difference between junior and senior residents regarding to marital status is statistically not significant (x2 = 2.8 and significance is 0.2) (Table 2).

Table (2): Marital status of junior and senior residents

	Single	Married	Divorced	Total	X2	Significance
Junior residents	17	22	0	39	2.8	0.2
Senior residents	9	22	1	32		
Total	26	44	1	71		

Level of significance at $p < 0.0$

A greater percentage of senior residents (34%) was doing recreational activities than junior residents (28%). The difference between senior and junior residents was statistically significant (x2 = 4.2 and significance is 0.04) (Table 3)

Table (3):Doing recreational activities among junior and senior residents

	Doing Recreational activities	%	Not doing Recreational activities	%	Total	%	X2	Significance
Junior Residents	20	28.2%	19	26.8 %	39	55%	4.2	0.04*
Senior Residents	24	33.8%	8	11.2 %	32	45%		
Total	44	62%	27	38%	71	100%		

*Level of significance at $p < 0.05$

Eighty percent of residents were not satisfied with the number of working hours, but the difference between junior and senior residents regarding to satisfaction with the number of working hours was statistically not significant ($x2 = 0.6$ and significance = 0.6) (Table 4).

Table (4): Satisfaction with working hours among junior and senior residents

	Satisfied with working hours	%	Not satisfied with working hours	%	Total	%	X2	Significance
Junior Residents	30	42.3%	9	12.7%	39	55%	0.6	0.6
Senior Residents	27	38%	5	7%	32	45%		
Total	57	80.3%	14	19.7%	71	100		

Level of significance at $p < 0.05$

Thirty seven residents were not satisfied with the number of calls per week, while 34 residents were not satisfied. There was no significant difference between junior and senior residents regarding to the number of calls per week (Table 5).

Table (5): Satisfaction with number of calls per week among junior and senior residents

	Not satisfied with No. of calls per week	%	satisfied with No. of calls per week	%	Total	%	X2	Significance
Junior Residents	24	33.8%	15	21.2%	39	55%		
Senior Residents	13	18.2%	19	26.8%	32	45%	3.1	0.1
Total	37	52%	34	58%	71	100%		

Level of significance at $p < 0.05$

It is expected to find a significant difference between the age of senior and junior residents. In this study there was a significant elder mean age among senior residents than junior residents (Table 6).

There was no significant difference between junior and senior residents regarding to the three mean values of the components of MBI (t-value = -0.8, -0.9, -1.5 and significance = 0.5, 0.4, 0.1) (Table 6).

Table (6): Comparison between junior and senior residents

As regards to the mean values of age and the 3 components of Maslach Burnout Inventory:

Mean values	Junior residents (No=39)	Senior residents (No=32)	t-value	Significance
Age (years)	26.6±1.5	28.9±1.8	- 5.8	0.000001*
Emotional Exhaustion	43.5±8	44.9±8	-0.8	0.5
Depersonalization	63.7±11.8	66.4±12.6	-0.9	0.4
Accomplishment	40.1±15.9	46±17.2	-1.5	0.1

*Level of significance at $p < 0.05$

Both junior and senior residents got high mean scores' values (27 or over), as regards to emotional exhaustion subscale (Figure 1), but the difference between the mean scores values was statistically not significant. In addition to this, they got also high mean scores' values (above 14), regarding to depersonalization subscale (Figure 2). On the

Contrary, they had poor social interaction "accomplishment subscale" (Figure 3).

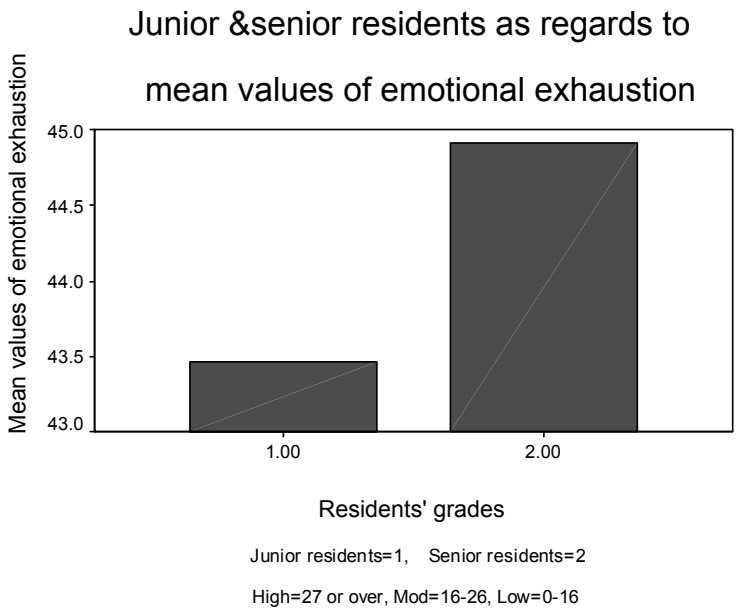
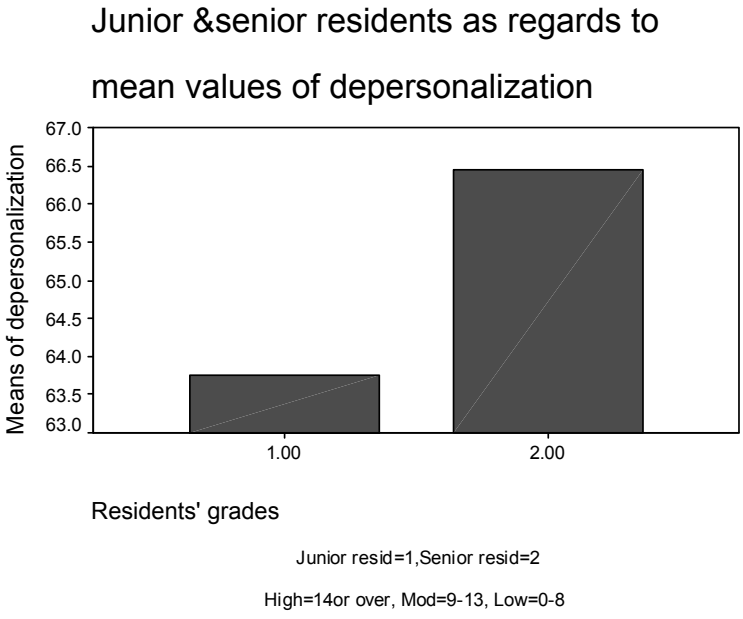


Figure (1)



Figure(2)

Figure(3)

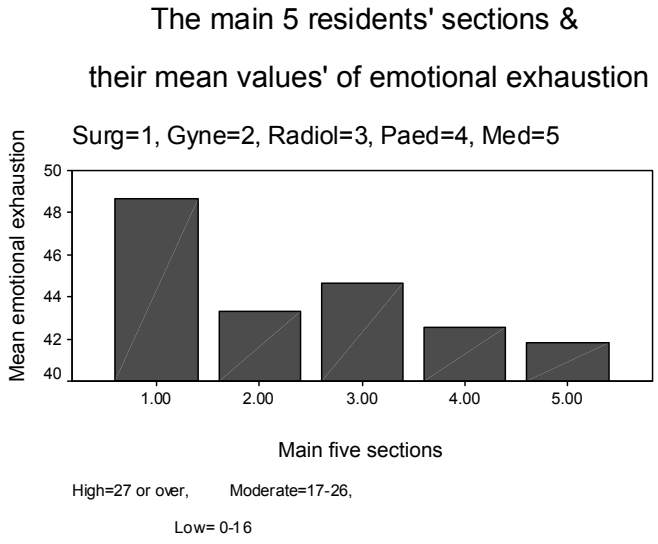
In this study, we found that these 71 residents could be classified into five main sections: 16 residents from surgery department, 10 residents from gynecology and obstetrics department, 9 residents from radiology department, 17 residents from pediatrics, and 19 residents from medical department. The difference between the mean ages of residents among the above mentioned five main sections was statistically not significant (ANOVA test was used, f = 1.2, p = 0.3). Medical residents had a significant lower mean values regarding to accomplishment subscale (35±10) than the other 4 main sections of residents (f = 2.2, p = 0.04) (Table 7). On the contrary, there were no significant differences between the five main sections as regards to emotional expression and depersonalization subscales (f = 1.7 and 1.5, p = 0.2 and 0.3) (Table 7).

Table (7): Comparison between 5 residents' sections as regards to the mean values of the 3 components of Maslach Burnout Inventory

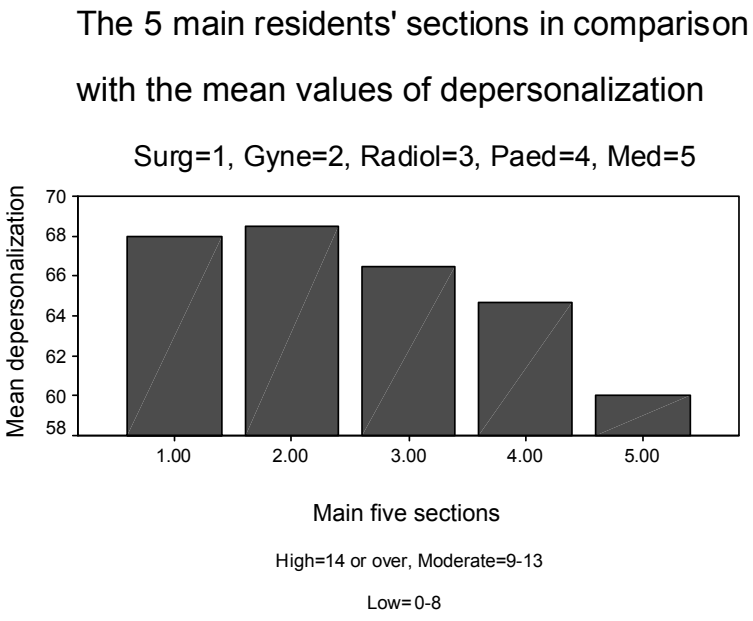
	Surg. Resid. (No=16)	Gyne. Resid. (No=10)	Radiol. Resid. (No=9)	Pedia. Resid. (No=17)	Med. Resid. (No=19)	f-test	Signifi-cance
Age	29.6±2.5	28.1±1.4	29.9±2.4	27.7±1.3	28.6±2.2	1.2	0.3
Emotional Exhaustion	48.7±7.8	43.3±7.7	44.7±6.5	42.5±8	41.88	1.7	0.1
Depersonalization	68±15	68.5±11.3	66.5±9.4	64.7±11.8	60.1±10.8	1.5	0.2
Accomplishment	46.8±17.8	50.8±18.2	39.8±19.3	44.4±17.2	35±10	2.2	0.04*

*Level of significance at $p < 0.05$

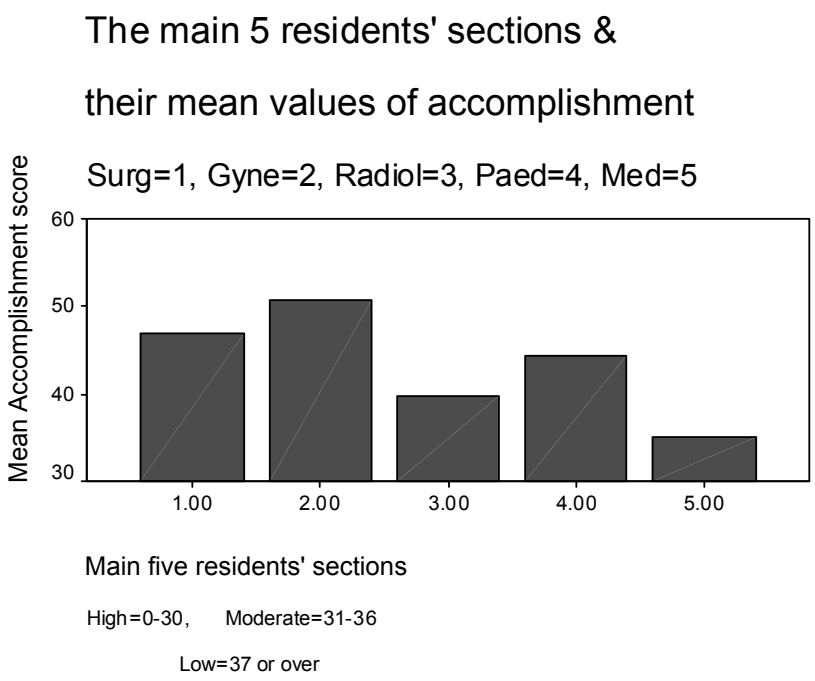
The five main sections of residents had high mean scores regarding to emotional exhaustion (27 or over) and depersonalization (14 or over) subscales of MBI (Figures 4 and 5). On the contrary, the five main sections of residents had low mean scores (37 or over) regarding to social interactions (accomplishment) (Figure 6). The mean values in figures 4,5,6 can show us that most of the residents in this study, were suffering from burnout syndrome.



Figure(4)



Figure(5)



Figure(6)

Surgical residents got significantly higher mean scores in two items of MBI than medical residents. These two items are sense of fatigue and dealing with their patients as objects. The test which had been used, was t-test (t = 2.4 and 3.5) respectively, significances were 0.02 and 0.001 (Table 8)

Table (8): Significant differences between medical and surgical residents regarding to the items of Maslach Burnout Inventory:

Item of MBI	Medical Residents (No = 36)	Surgical Residents (No = 35)	t-test	Significance
Sense of fatigue	3.5±2	4.6±1.7	-2.4	0.02*
Dealing with patients as objects	0.7±1.2	2.1±2	-3.5	0.001*

*Level of significance at $p < 0.05$

Discussion:

To our knowledge, the first study comparing burnout among residents across medical specialties was at Wayne State University and in South Carolina in 2004 (Balon R, et al 2004). The lack of findings of statistically significant differences in

burnout rates among specialties may be due to low and perhaps differential response rates. It is plausible that those residents who felt burned out were more or less likely to respond, even to three mailings. The findings of comparable burnout rates among family medicine residents at Wayne State University and in South Carolina(Michels PJ, et al 2003) and internal medicine residents at Wayne State University and the University of Washington (Shanafelt TD et al, 2002) lead us to believe, although with caution, that the results might be generalized to settings outside of Wayne State University, particularly in Western communities. The first study is limited by the low response rate and small numbers of residents in some specialties, which may have affected the findings. In a survey of medical students' attitudes and concerns regarding possible repercussions of completing a depression survey, only 48% finished the survey (40% of those completed the depression inventory with 10% admitting to recording dishonest answers and 19% admitting to concerns about the research(Levine RE, et al 2003). These results are in accord with verbal feedback from residents to the first author (Balon R, et al 2004), expressing concerns of confidentiality and potential negative consequences of self-reporting.

In our study, nearly all the residents of the Saudi Board Program at King Abdul-Aziz Medical City were welcoming to participate in this study, as its results will be represented in front of some authority figures of the Saudi Board Program on the Residents' Day. In the present study, there were no significant differences between senior and junior residents as regards to the mean values of the three components of MBI (Table 6). This can be explained by the support which might be given by senior residents and staff. On the contrary, in the above mentioned American studies, they found that junior residents had higher rate of burnout, which may indicate that they are a vulnerable group. Special attention by program directors may be needed to reduce this high rate of burnout.

In the present study, we found that surgical residents had significantly higher mean score value regarding sense of fatigue than medical residents. To explain this, we think surgical residents have to practice many clinical surgical skills, in addition to studying theoretical medical and surgical curriculum. All of us know that, a good surgeon is a good decision taker and maker, which add more responsibility to surgical residents. All these responsibilities need extra times and efforts to be achieved. That is why surgical residents are more fatigued and overwhelmed than medical residents. Fatigue is a common complaint in the general and working population, with a reported prevalence varying from 7% to 45%. Fatigue can best be understood as a continuum, ranging from mild complaints frequently seen in the community on the one hand to severe, disabling fatigue, such as chronic fatigue syndrome on the other.' When fatigue among employees becomes severe and persistent, it may lead to long term sick leave and work disability. Conceptually linked with fatigue and absenteeism is the phenomenon of burnout. In general, burnout can be described as a persistent, negative, work related state of mind characterized by work related emotional exhaustion and accompanied by distress, (perceived) reduced effectiveness, decreased motivation, and dysfunctional attitudes and behaviors at work. Burnout symptoms are mostly psychological and burnt out workers often causally attribute their complaints to problems at work,

blaming their jobs for their condition. A conservative estimate of the prevalence of "clinical" burnout is 4.2% in the working population.' Like persistent fatigue, burnout can lead to long term sick leave. However, it is important to realize that persistently fatigued workers are not burnout by definition, and that burnt out workers might not experience fatigue as a major complaint.

In that sense, it is of great importance to identify the determinants of recovery in fatigued employees: if causal attributions can determine the course and outcome of fatigue complaints in employees, it might be an indication that early prevention of chronic fatigue lies partly in alterations of the labeling of fatigue complaints, for example with the use of cognitive behavioral techniques (Huibers et al, 2003).

In our study, there were no significant differences between sex, marital status, numbers of working hours and numbers of on calls per week as regards to junior and senior residents. Multiple studies shows no significant associations between variables such as sex, marital status, location of housing, age and the three MBI "components' subscales (Elnagar et al, 2001, Leiter and Harvie 1996). These findings differ from other studies, which found negative correlations between age, years of experience and burnout (Maslach & Jackson, 1981; Meadow, 1981; Randall & Scott, 1988). In a study on correlations between age and acquired work experience and burnout, in a sample of nurses working in an AIDS care unit versus a sample of nurses working in an oncology unit, it was found that older age was a protective factor towards the development of burnout. On the contrary, acquired work experience was not a protective factor in the development of burnout (Bennett, 199l). Moreover, only a weak significant correlation between the length of work with HIV-infected patients and the 'Depersonalization' scale was found. Instead three predictive variables: 'Peer relationship'. 'Social reward, 'Grief & Loss' correlated significantly with the three MBI components scales. As expected, 'Peer relationship' and 'Social reward' were protective (negative correlation) against burnout in the 'Emotional exhaustion' and 'Depersonalization' MBI subscales. 'Grief & loss', on the contrary, had positive correlations with burnout in the 'Emotional exhaustion' and 'Depersonalization' subscales and a negative correlation with burnout in the 'Personal achievement or accomplishment' MBI subscale. As described in the results, the length of work variable is a predictor of clinical burnout levels on the 'Emotional exhaustion' and 'Depersonalization' subscales and not, obviously, on the 'Personal achievement or accomplishment' subscale.

Future studies on burnout syndrome among medical residents should find out the role of the personal characteristics of residents, the style of their relationship with patients and the individual perception of stress and of work stressors as etiological factors in occurrence of burnout syndrome.

We have to mention that there are some studies about burnout syndrome among certain residents' specialties like anesthesia (Nyssen AS, et al 2003), intensive care, gynecology & obstetrics, orthopedics, internal medicine (Geurts S, et al 1999) (Shanafelt TD, et al 2002) family medicine (Lemkau J, et al 1994) and psychiatry. The results of one of the above mentioned studies (Nyssen et al, 2003) showed that 40.4% of the anesthetists were suffering from high emotional exhaustion; the highest

rate was in young residents under 30 years of age. These results are particularly alarming. Moreover, first-year residents did not feel as empowered as the others. Surprisingly, fourth-year anesthetists also showed a low score for empowerment. It is well recognized among Belgian anesthetist supervisors that the third year of training is particularly critical because this is when the trainees start to work on their own in the operating room, calling for help when problems occur. In fact, the third-year anesthetists showed the highest stress scores in the above mentioned study, but there were no significant differences between the six training levels. The lower self-confidence score found in fourth-year residents may come from this critical year. Results also indicated that 23% of trainees felt under-- supervised and some authors have demonstrated that support can alleviate job stress (Collier V, et al) (21). Together, the lack of empowerment and the lack of support, by decreasing the individual's ability to cope with stressful situations, could explain the high score for emotional exhaustion found in the young anesthetist group. These details about burnout syndrome among different years of anesthesia residency graduation can be studied in different residents' specialties as future studies.

Summary and conclusions:

In this study we found that:

-Junior Medical residents are the least who suffer from burnout, followed by seniors' medical residents.

-Obstetrics, Gynecology and Surgical residents are the most sufferer from burnout symptoms among all specialties included in this study.

-Number of working hours, on calls per week, & residents who live away from their places of work, all are issues need to be discussed with the decision makers.

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فحص ظاهرة الاحتراق بين الأطباء المقيمين العاملين بالتخصصات الطبية المختلفة

Motives for Substance Use Disorders: A Trans-cultural Study

Ismail K., Molokhia T., and Saadani M.

Abstract:

The causes of substances abuse may be of greater importance in different culture. The aim of this study was to compare between Egyptian and Saudi cultures regarding to the causes and the socio-demographic data in substance abusers of these two countries. Thirty two abusers from Mecca and Jeddah, Saudi Arabia, were chosen randomly, their mean age was 33.6±13.6 years old. Another 32 abusers from Alexandria, Egypt were also chosen randomly. Their mean age was 25.3±6.4 years. There were 9 females as benzodiazepine abusers in the Saudi sample, substance abuse causes questionnaire was applied on every abuser participated in this study. More than one third of abusers were students. Mean values of cognitive, emotional, somatic causes and total scores of the scale were not significantly different between Egyptian and Saudi samples, t-test were 0.1, 1.6, 1.1 and 1.2 respectively while p = 0.9, 0.1,0.3 and 0.3 relatively. The Egyptian abusers showed a significant abuse of opioids ($X^2$24.5, p = 0.00001), while the Saudi abusers abused benzodiazepines and stimulants significantly more than the Egyptian abusers (X^2 = 28 and 9 respectively and p = 0.000001 and 0.005 relatively). The drivers or causes of substance abuse are similar in Egypt and Saudi Arabia, Egyptian abusers abuse opioids more than the Saudi abusers while Saudi abusers abuse benzodiazepine and stimulants more than Egyptian abusers.

Introduction:

The reasons for the initiation of substance use disorders may be of greater importance at different ages and in different cultures (Oyepeso A, 1994). For example, the consumption of sedatives and benzodiazepines by older people may begin as self mediation. Drugs may be taken to overcome fatigue or to enhance the appetite and sexual performance. Drugs may be taken for religious purposes purposes as an aid to mediation or to induce mystical states (Robinson TE & Berridge KC, 2003).

Some authors classified the causes of substance abuse into: causes in substance itself, individual personality and society. Other authors divided the motives for substance abuse into social, psychological and environmental factors. Some psychologist divides the causes of substance abuse into cognitive, emotional and somatic causes (Combag HS et al., 2001, Cardinal RN et al., 2002, Dickinson A and Balleine B, 1994). The impact of new drugs and new technologies in different culture is considered. Around 1980, the discovery that heroin could be inhaled and sublimated off the surface of heated tin foil undoubtedly contributed to the explosion of heroin abuse at that time in Britain (Strang & Gossop 1993). During the 1980s the North West Frontier of Pakistan has been one of the major producer regions for black market heroin for export around the world and despite a long history of culturally bound smoking of the opium poppy, the refined product (heroin) is decimating the young male population with current estimates that there are in excess of one million young men who have recently become addict to heroin in Pakistan (Gossop M, 1989, Abdel-Gawad TMS and Osman MI, 1996).

The cathinoids which are alkaloids derived from khat, that is native to East Africa and the Western south part o the Arabian Peninsula, where it grows as evergreen shrub or small tree. The primary active psychoactive ingredients in that are cathinone and cathine, two central nervous system stimulants. A systemic analog of cathinone and metcathinone appeared in the USA for the first time in 1991. In Egypt cannabinoids have always been more widely abused than opioids. Also the wide-spread availability of bango and its cheap price made helped in the persistence of cannabinoids as the most widely abused illicit drug in Egypt till now. A study done to determine why do people abuse drugs in certain categories of drug-abuser found that among high school and university male students the main causes for cannabis abuse were having fun and sharing in a social events as well as sharing peers, while the use of other psychoactive drugs (stimulants and benzodiazepines) was mainly for the relief of physical problems and fatigue followed by the desire to study particularly at the time of exams. However, regarding laborers it was found that they abused cannabis for the same causes as students. On the other hand, they used psychoactive substances for the relief of physical problems and fatigue as well as for getting rid of psychological and social problems (Saueif et al, 1988).

The aim of this study was to compare between two samples of substance abusers one sample was from Alexandria, Egypt and the other one was from Mecca and Jeddah, Saudi Arabia – as regards to socio-cultural demographic data and the causes of substance abuse either emotional, cognitive or somatic and sexual causes.

Methods:

Thirty two substance abusers were chosen randomly from the psychiatric patients who attended the out patient psychiatric clinics in three governmental hospital of Mecca and Jeddah (Saudi Arabia).

The researchers chose every third substance abuser patients during the period from the 1st of January to the end of June, 2003. Fifty three Saudi substance abusers refused to participate in this study. Another 32 substance abusers were randomly chosen from two private psychiatric hospitals in Alexandria, Egypt.

They were chosen from the in-patients randomly (every third admitted patient) during the same above mentioned periods of time. Sixty one substance abusers refused to participate in this study from Egyptian substance abusers.

A questionnaire about causes of substance abuse was applied on every substance abuser, who participated in this study (Askar A, 1989). An informed consent was taken from every substance abuser, who participated in this study. The questionnaire is consisted of 33 items, which cover the different causes or motives for substance abuse. The author of this questionnaire mentioned 3 types of causes for substance abuse: Cognitive emotional and somatic causes. The reliability of this questionnaire was 0.57 using Sperman and Brown test and its validity was 0.25 (using kappa). This questionnaire is subjective which can be applied individually or in groups. In cases of illiterate patients the researcher, could read the items and check correct in front of chosen items consisted of the illiterate individual. The time needed to complete this questionnaire is ranged from 8-12 minutes.

Socio-demographic data and the time of substance abuse were collected from all substance abusers who participated in this study.

All substance abusers who participated in this study were fulfilling the criteria of diagnostic and statistical Manual of Mental disorders number IV-TR. (American psychiatric Association 2000). All substance abusers who participated in this study had no psychotic disorders and no physical illnesses like diabetes mellitus ischemic heart disease, cancer, … etc.

Statistical analysis:

The program of SPSS + PC was used to analysis the data. T-test was used to compare between two quantitative means while Chi-square was used to compare between qualitative means.

Results:

The mean age of the Egyptian sample of substance abusers was 25.3±6.4 years old while the mean age of the Saudi sample was 33.6±13.6 years old. The difference between these 2 means was statistically significant (t-test = 3.1 and p = 0.003). The 95.0% confidence interval of the difference was 3-13.6 years. The mean duration of substance abuse among the Egyptian abusers was 4.2±3.4 years, while that for the Saudi abusers was 4.6±2.7 years. The difference between these two means was statistically not significant (t-test = 0.5 and p = 0.6). The 95% C.I. was ranging from –1.2 to 1.9 years (Table 1).

Table (1): Comparison of mean age and mean duration of substance abuse between Egyptian and Saudi samples

Mean	Egyptian sample	Saudi sample	t- test	Significance	95% confidence interval
Variables	Mean ± SD	Mean ± SD			
Age (years)	25.3±6.4	33.6±13.6	3.1	0.003*	3-13.6
Duration of substance of substance abuse (years)	4.2±3.5	4.6±2.7	0.50	0.60	-1.2-1.9

Level of significance is at $p < 0.05$

There were 9 females out of 32 substance abusers in the Saudi Sample while there was no female in the Egyptian sample. All these females were house wives and benzodiazepines and Saudi substance abusers as regards to gender was statistically significant ($X^2=10$ while $p = 0.001$). (Table 2).

Table (2): Sex distribution between Egyptian and Saudi samples of abusers:

Nationality / Sex	Egyptian abusers	Saudi abusers	X2	Significance
Female	0	9		
Male	32	23	10	0.001*
Total	32	32		

Level of significance is at $p < 0.05$

In the present study, there were 23 students, 10 semiprofessionals, 8 professionals, 6 laborer workers, 5 soldiers and 3 not working. The difference between Egyptian and Saudi substance regarding to occupations was statistically significant ($X^2 = 29.6$ & $p = 0.00001$) (Table 3).

Table (3): Comparison of occupations between an Egyptian and Saudi substance abusers' samples.

	Egyptian samples No= 32	Saudi sample No = 32	Total	X^2	Significant
Professional	8	0	8		
Semi-professional	6	4	10		
Soliders	0	5	5		
House-wives	0	9	9	29.6	0.00001*
Students	16	7	23		
Laborer workers	2	4	6		
Not-working	0	3	3		
Total	32	32	64		

Level of significance is at $p < 0.05$

Forty two substance abusers out of 64 were single, while only 17 abusers were married, 3 were divorced and 2 were widowed. The difference between Egyptian and Saudi abusers regarding to marital status was statistically not significant ($X^2 = 7.6$ while p 0.06) (Table 4).

Table (4): Comparison of marital status between an Egyptian and Saudi substance abusers' samples.

	Egyptian samples No= 32	Saudi sample No = 32	Total	X^2	Significance
Single	26	16	42	7.6	0.06
Married	5	12	17		
Divorced	1	2	3		
Widowed	0	2	2		
Total	32	32	64		

Level of significance is at $p < 0.05$

Mean values of cognitive emotional, somatic causes and total scores of substance abuser causes questionnaire were not significantly different between Egyptian and Saudi samples, t-test were 0.1, 1.6, 1.1 and 1.2 respectively, p = 0.9, 0.1, 0.3 and 0.3 relatively. The mean values of total scores of the questionnaire for Egyptian and Saudi samples were 8.5 ±6.2 and 10±3.6 relatively, the 95% confidence for the difference was 01.1 to 4. (Table 5).

Table (5): Comparison of cognitive emotional somatic and total mean scores-constitutes of substance abuse causes questionnaire-between an Egyptian and Saudi samples

	Egyptian sample No = 32	Saudi sample No = 32	t- test	Significance	95% confidence interval
	Mean ± SD	Mean ± SD			
Cognitive causes	3.1± 2.9	3.1±2.1	0.1	0.9	-1.2-1.3
Emotional causes	3.2±2.0	3.9±1.5	1.6	0.1	-0.2-1.6
Somatic causes	2.2±3.2	2.9±1.6	1.1	0.3	-0.6-2
Total	8.5±6.2	10±3.6	1.2	0.3	-1.1-4

Level of significance is at $p < 0.05$

The Egyptian sample showed a significant abuse of opioids than Saudi sample (X^2 = 24.5, p = 0.00001). Twenty one Egyptian abusers out of 32 substance abusers were abusing different types of opioids in the form of heroin, opium, codeine and pethidine. Only two of the Saudi sample were abusing opioids. Eight Egyptian abusers were abusing cannabinoids in the form of cannabis and Bango while 3 Saudi abusers were abusing cannabis. The difference

between Egyptian and Saudi samples was not statistically significant regarding to cannabinoids abuse (X^2 = 2.7 and p = 0.09). Three Egyptian abusers were abusing alcohol while 4 Saudi patient were abusing it. The difference as regards to alcohol abuse between 2 samples was statistically not significant (X^2 = 0.2 and p = 0.7). Twenty one Saudi were abusing benzodiazepines while only 2 Egyptians were abusing them. The difference between Egyptian and Saudi samples regarding to benzodiazepines abuse was statistically significant (X^2 = 28.0 and p = 0.000001). Nine females were abusing benzodiazepines from the Saudi sample. Twelve Saudi patients were abusing stimulants mainly in the form of amphetamines (Pemoline magnesium). They call it "white". Two Egyptians were abusing "Maxitone forte" which contains amphetamines. There was a statistically significant difference between Egyptian and Saudi samples regarding to amphetamine abuse (X^2 = 9.0, p = 0.005) (Table 6).

Table (6): Comparison of occupations between an Egyptian and Saudi substance abusers' samples.

Individuals	Egyptian samples		Saudi sample		Total	X^2	Significant
Substance	Abusers	Not-abusers	Abusers	Not-abusers			
Opioids	21	11	2	30	64	24.5	0.00001*
Cannabinoids	8	24	3	29	64	2.7	0.09
Alcohol	3	29	4	28	64	0.2	0.70
Benzodiazepines	2	30	21	11	64	28	0.000001*
Stimulants	2	30	12	20	64	9	0.005*

Level of significance is at p < 0.05

Discussion:

Many studies have shown that there is indeed an increased incidence of personality disorder among substance abusers for example application of MMPI to opiate abusers showed that they scared higher than expected for psychopathic deviance (Cami J et al 1991). However, when Eysenck personality inventory was applied to opiate abusers, they scored higher on neuroticism than normal (but lower than neurotic or alcoholic patients). Moreover, it was found that 73-90% of opiate addicts were diagnosed as having some sort of personality disorders. For the above mentioned reasons, we could not exclude neurotic and personality disorders co-morbid with substance abusers who participated in this study (Graig RJ, 1982).

A problem which faced us in the present study was that, we selected sub-groups of substance abuse subjects from governmental and private hospitals. These abusers are probably unrepresentative of the drug dependent population as a whole (Iqbal N, 2001). Moreover, the sample of substance abusers from Saudi Arabia did not include abusers from specialized hospitals for addiction i.e. (Al-Amal

Hospitals). Not only this, but also a relatively small number of substance abusers in both Egyptian and Saudi samples should be considered.

A replication of this study by using larger samples may be needed in the future to understand, assess the problem of substance abuse in these 2 different cultures in a better way, and to prepare suitable programs which will help in combating the dangerous problem of substance abuse.

One of the outstanding findings in this study is the significantly higher mean age of Saudi substance abusers. This may be the effect of extended families which are common in Saudi communities. The grand parents and parents are controlling the young adult and this may be one explanation of this phenomenon. Another explanation is that a good number of Saudi abuses stimulants, which are expected to be abused in an elder age where the sleep is induced by benzodiazepines at night and stimulants are used to increase activities and prevent sleeping and keeping awake during wedding nights and driving for a long distance for some abusers (Amir T, 2001). Some of them abuse stimulants to increase their sexual drives (AL-Nahedh N, 1999). In the Egyptian sample, the absence of extended family, the absence of the role of grand parents and even the weak control of parents in some nuclear families may be behind the younger mean age of substance abuse among the Egyptian abusers (Anthony JC et al, 1995).

Another strange finding in this study is the significantly higher number of female in Saudi sample. This may be due to the bias in selecting the samples as we mentioned above. Another explanation is that all 9 substance abusers' Saudi females were benzodiazepines' users. They use them mainly as sleeping pills. Tolerance to them occurred with running the time. A previous study in Jeddah, showed the presence of heroin dependence complications among 3 females (Othman A and Shawoosh M, 2003).

This is consideration an iatrogenic benzodiazepines abuse, which is common in developed countries like France and USA. The weather in Mecca is very hot nearly during the whole year, overcrowded; noisy and shopping is continuous for 24 hours around Al-Harm -due to Hajj and Omrah. Because of all the previously mentioned reasons, insomnia is common and drive to abuse sedatives and hypnotics (Mohit A, 2001). According to Roth, approximately "70%" of the prescriptions for benzodiazepines and sedatives are written for women Moreover, women are twice as likely as men to be addicted to prescription drugs in combination with alcohol" (Roth, 1991). Alcohol is prohibited in Islamic religion, that is whey a few number of abusers, abused. Alcohol in both Egypt and Saudi Arabia.

A large number of abusers in the present study were students (more than one third of the whole samples). In any community students are the real future of its. So, this study gives us an alarm against the dangerousness of substance abuse in our developing countries.

The drives, the causes or the motives for substance abuse were similar in Egyptian and Saudi communities. For this reason, the programs and the planning for future prevention and management of this hot and dangerous topic can be shared between the responsible governments and authority figures in both Egypt and Saudi Arabia.

Opioid abuse is more significantly common among the Egyptian sample than the Saudi one. This might be due to the selection of Saudi sample from governmental general hospitals and not from specialized hospitals in substance abuse like (Al Amal Hospitals) where, opioids abusers especially heroin are admitted there for detoxification. This again reminds us that in future studies we have to take larger samples to represent abusers from different cities and different types of hospitals, schools, universities, institutes, factories and even prisons.

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Burnout Syndrome among Resident Physician in Suez Canal University Hospital

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Abstract

Background: Burnout is a syndrome of emotional exhaustion, depersonalization and a sense of low personal accomplishment. Little is known about burnout or its demographic perspectives in Egyptian residents. Objective: To determine the prevalence of burnout among residents and explore its demographic perspectives. Design: Cross-sectional study using an anonymous handled survey. Setting: University-based residency program in Suez Canal University Hospital. Participants: 84 residents. Measurements: Burnout was measured by the Maslach Burnout Inventory and was defined as scores in the high range for medical professionals on 2 or more of the subscales. An inventory developed for this study assessed self-reported sources of stress in job setting and involvement with people. Results: Of 84 (72.4%) responding residents, 53 (63.1%) met the criteria for burnout. None of the burnout dimensions was significantly associated with sex. Only lack of personal accomplishment was significantly associated with marital status and number of work-hours per week (p value < 0.05). Burnout domains were significantly associated with sources of stress. Conclusion: Burnout was common among resident physicians and mainly related job setting and involvement with people.

Introduction

The word "burnout" means to be depleted. It is associated with the worker's physical and psychological exhaustion when he wears his resources out trying to cope with the difficulties of his everyday working activity. The word burnout refers to the "bad mood, the daily irritation, the prostration, the feeling of emptiness, the disillusion, and the powerlessness many workers feel, particularly those in the helping professions (Unknown, 2002). Within the job stress-illness literature, the study of burnout has started since 1964 (Snibbe et al, 1989). Since Freudenberger (1974) used the term burnout, it has mainly been used to describe a state of physical and emotional exhaustion whose characteristics have been mostly applied to human services professionals, within which health staff is included. Burnout can be described as a specific type of job stress, which influences job-related affective well being (Schaufeli & Buunk, 1999). Burnout, a widely studied syndrome, has been defined by Barnett et al (1999) as comprising three factorially distinct symptoms: emotional exhaustion, decreased sense of professional efficacy, and cynicism. According to Maslach et al (2001), burnout is a syndrome defined by the 3 principal components of emotional exhaustion, depersonalization, and diminished feelings of personal accomplishment. Earlier studies on physicians have reported a burnout rate of 30% to 40% (Henderson, 1984). Some particular subgroups, such as infectious disease physicians, have been subsequently found to have burnout rates as high as 43.5% (Deckard et al, 1992). A study by Fields et al (1995) reported that 36% of physicians in pediatric critical care were classified as at risk for burnout, and 14%

were burned out. The evidence, albeit from small and generally localized samples, suggests that the components of burnout may be common among practicing physicians, with 46% to 80% reporting moderate to high levels of emotional exhaustion, 22% to 93% reporting moderate to high levels of depersonalization, and 16% to 79% reporting low to moderate levels of personal achievement (Lloyd et al, 1994). Studies of medical residents have yielded similar results (McCue and Sachs, 1991). In a survey of 119 academic obstetrics and gynecology department chairs in the United States and Puerto Rico (response rate, 91%), Gabbe et al (2002) found that 56% of respondents demonstrated high levels of emotional exhaustion, 36% had high levels of depersonalization, and 21% reported low levels of personal accomplishment. Mirvis et al (1999) reported an increase in the prevalence of high levels of burnout (from 25.3% in 1989 to 38.1% in 1997) in a cohort of 83 administrators of the Department of Veterans Affairs medical centers. The specific consequences of physician burnout are less well known. Mirvis et al (1999) identified loss of job satisfaction as both a primary consequence of burnout and a contributor to its further progression. Similarly, Grunfeld et al (2000) reported that emotionally exhausted Canadian oncologists were more likely to consider changing jobs or reducing work hours. Burned-out residents were also significantly more likely to indicate that they had been responsible for 1 suboptimal patient care practice at least weekly or monthly compared with non–burned-out residents (Shanafelt et al, 2002). Research over the last three decades has shown that the consequences of burnout are not just limited to the individual's subjective experience, but also to various organisational outcomes. Burnout has been associated with reduced organisational efficiency and work related problems such as employee turnover, low morale, poor quality of care, lowered productivity, absenteeism and interpersonal problems (Rosse et al, 1991; Levert et al, 2000).

The study of burnout, therefore, becomes crucial for identifying the dimensions of the problem among Egyptian residents, to improve their quality of life and optimising the care they aught to give to their patients.

Aim of the work This study aim to identify the burnout syndrome among the resident physicians in Suez Canal University Hospital. Specifically, the study will determine; the prevalence of burnout syndrome among the residents, sources of stress and the Effects of gender susceptibility among them

Subjects and Methods

A descriptive cross sectional study was held targeting resident physicians at Suez Canal university hospital in Ismailia.

Sampling and sample size:

** Sample type: simple random sample.

** Sample size: The sample size was determined using the following equation:

$S = [Z^{\alpha/2} / \Delta]^2 * P (1-P)$ (Dobson, 1984)

Where: -

$Z^{\alpha/2}$ (confidence level) = 1.96

Δ (width of confidence interval) = 0.05

P (prevalence) = 30% (Henderson, 1984)

S (sample size) = 323

As the population is known and is small (there are 180 resident physicians in

University Hospital of Suez Canal University according to the hospital files), finite population correction was calculated as follows:

$N = S / [1 + (S - 1) / N]$ (Israel, 1992)

Where: -

N (finite population size) = 180

N (adjusted sample size) = 116

The following inclusion criteria were applied:

Physicians who have not got their Master Degree yet.

Residents who have been working for one year or more.

Residents who have regular attendance and shifting schedules.

Measurement instruments:

To achieve the objectives of this study, a questionnaire was used; formed of three parts:

1- Socio-demographic data: age; sex; marital status and average number of working-hours per week.
2- Part adopting the Arabic Translation (Appendix B) of Maslach Burnout Inventory (MBI) (1996) specially tailored to apply to physician. (Appendix C),
3- Part including an inventory of the sources of stress for the resident physicians. (Appendix D)

Procedure:

Questionnaire was tested for applicability and practicability in a pilot study, and any inconsistencies were removed.

Each physician was handled a 3-part questionnaire and given a one-week period to complete it. The order of presentation of the SOURCES OF STRESS and the MBI was counterbalanced to minimize any potential order effect.

After the end of the one-week period; the physician was considered as "non – respondent" if the questionnaire was not returned.

Scoring and interpretation of results:

1- Maslach Burnout Inventory (MBI): (1996)

The MBI is designed to assess the three aspects of burnout syndrome: emotional exhaustion (EE) (statements No. 1, 2, 3, 6, 8, 13, 14, 16, and 20), depersonalization (DP) (statements No. 5, 10, 11, 15, and 22), and lack of personal accomplishment (PA) (statements No. 4, 7, 9, 12, 17, 18, 19, and 21). A separate subscale measures each aspect.

Burnout is conceptualized as a continuous variable, ranging from low to average to high degrees of experienced feeling.

A high degree of burnout is reflected in high scores on EE and DP subscales and in low scores on PA subscale.

An average degree of burnout is reflected in average scores on the three subscales.

A low degree of burnout is reflected in low scores on EE and DP subscales and in high scores on PA subscale.

At present, scores are considered high if they are in the upper third of the normative distribution, average if they are in the middle third, and low if the are in the lower third. The numerical cut-off points are shown in the following table: (MBI Manual, 1996)

Range of Experienced Burnout

MBI Subscales	Low (Lower third)	Average (Middle third)	High (Upper third)
EE	≤ 16	17-26	≥ 27
DP	≤ 6	7-12	≥ 13
PA	≥ 39	38-32	≤ 31

(N.B. PA is measured in the opposite direction to EE and DP)

The MBI scores for a group of respondents may be treated as aggregate data. Means (M) and standard deviations (SD) for each subscale are computed for the entire group and can be compared to the normative data in the following table:

MBI Subscales

	EE	DP	PA
M	20.99	8.73	34.58
SD	10.75	5.89	7.11

(MBI Manual, 1996)

A participant was considered to meet the study criteria for burnout if he or she got a "high" score on at least 2 of the three dimensions of MBI.

2- Sources of Stress (SS):

The Sources of Stress questionnaire is designed to assess the two main sources of stress: job setting (JS) (statements No. 1, 7, 8, 9, 11, 12, 15, 16, 17, 19, 20, 21, 22, 23 and 24) and involvement with people (IP) (statements No. 2, 3, 4, 5, 6, 10, 13, 14, and 18). A separate subscale measures each aspect.

Sources of Stress are conceptualized as a continuous variable, ranging from low to moderate to high degrees of experienced feeling.

- A high-degree source of stress is reflected in high scores on JS and IP subscales.
- An average-degree source of stress is reflected in averages scores on the two subscales.
- A low-degree source of stress is reflected in low scores on JS and IP subscales.

At the present study, scores were considered high, average, and low according to the following empiric numerical cut-off points as shown in the following table:

Range of Experienced Stress

SS Subscales	Low	Average	High
JS	≤ 25	26-50	≥ 51
IP	≤ 15	16-30	≥ 31

The SS scores for a group of respondents may be treated as aggregate data. Means (M) and standard deviations (SD) for each subscale are computed for the entire group.

Statistical analysis:

Responses from physicians will be statistically analyzed by use of latest version of SPSS available. Significance tests (Chi square) will be applied and significance will be determined when $p<0.05$. For presentation purpose, only the significant or the more prevalent options of the findings will be presented.

Results:

Out of the 116 residents handled the questionnaire; 84 returned it within the time limit of one week, giving a response rate of 72.4%.

Respondents:

The socio-demographic characteristics of the respondents (Table 1) were such that most were males (76.2%) and single (63.1%). The mean of working hours per week of the group was 83.6 work-hours/week (SD 35.5).

Burnout

Presently, normative data of the MBI burnout dimensions of emotional exhaustion, depersonalization and personal accomplishment exist for medical practitioners. Table 2 provides the mean and standard deviation of all of the three dimensions of burnout for this population of resident physicians along with those previously reported by Maslach, Jackson and Leiter (1996) from normative data of medical practitioners. As shown in Table 2, the mean burnout sub-scale scores of emotional exhaustion (32.74) and depersonalization (14) are much higher than the normative data from other medical practitioner populations.

However, the mean sub-scale score on the dimension of personal accomplishment (35.03) is almost equal to those of the other populations, indicating that, on average, the resident physicians in the present sample are still experiencing the sense of accomplishment to a more or less similar degree as the comparison groups.

Mean score for emotional exhaustion is in the "high" range (≥ 27), and the same for depersonalization (≥ 13). For personal accomplishment, the mean score is in the "average" burnout range (38-32) (Table 3).

In terms of the personal impact of work-related stress, work-induced "high" emotional exhaustion was identified in 75% of resident physicians, depersonalization in 60.7%, and lack of personal accomplishment in 27.4% (Table 3).

More than 25% of the respondents scored "high" on only one dimension of Maslach Burnout Inventory (MBI), 50% scored

"high" on any two of the dimensions of MBI, and 13.1% scored "high" on the 3 dimensions altogether. So, 63.1% of participants met study criteria for burnout (a "high" score on at least 2 of the three dimensions of MBI).

Table 4 provides the mean and standard deviation for each of the 2 dimensions of sources of stress (SS) studied for this sample of residents. Unfortunately, no normative data are currently available; therefore, it is not possible to make direct comparisons of scores obtained from the population in this study with a representative norm group.

However, the mean scores for job setting (48.85) and involvement with people (26.73) as sources of stress are in the "average" range for both dimensions (table 5).

Table 5 also shows that all the responding physicians are either averagely or highly stressed by their job settings.

Gender perspectives:

Work-induced emotional exhaustion (EE), depersonalization (DP), and lack of personal accomplishment (PA) are independent of sex (Tables 6).

The table shows that 75 % of the males and 75% of the females participating in this study score "high" on emotional exhaustion, so they are equally expressed in the "high" range of this dimension of MBI. Lack of personal accomplishment, as well, seems to be almost evenly distributed among male and female resident physicians.

However, it is shown that male residents are relatively more depersonalized by the effect of work (62.5%) than their female counterparts (55%). However, the difference is statistically insignificant.

Meanwhile, experiencing work-related stress associated with job setting and involvement with people is also independent of sex.

Table (6) shows that female residents are relatively more at the "high" range of job setting- induced stress (55 %) than their male colleagues (39.1 %). Also, female residents are relatively more at the "high" range of involvement with people - induced stress (45 %) than their male colleagues (29.7 %). But in either case, the difference between both sexes is statistically insignificant.

Other socio-demographic perspectives:

Work-induced emotional exhaustion and depersonalization are independent of marital status (Table 7). However, lack of personal accomplishment proved to be significantly associated with marital status.

This table shows that married residents are more at the "high" range of emotional exhaustion (83.9%) than their single colleagues (69.8%). Also, shows that married residents are more at the "high" range of depersonalization (67.8%) than their single counterparts (56.6%). But the difference between the two groups was statistically insignificant.

However, a significant relationship between marital status and lack of personal accomplishment is shown in this table. Single participants are more at the "high" range (28.3%) than their married colleagues (25.8%). However, while 43.4% of the single residents in the study sample being in the "low" range for lack of personal accomplishment, only 19.4% of the married are in the "low" range.

At the same time, experiencing work-related stress associated with job setting and

involvement with people is independent of marital status.

Table (7) shows that single (43.4%) and married (41.9%) participants experience "high" job setting-induced stress almost equally. Also, shows that single (33.9%) and married (32.3%) participants are in the "high" range of involvement with people-induced stress almost equally.

Work-induced emotional exhaustion and depersonalization are independent of the number of work-hours per week (Table 8). However, lack of personal accomplishment proved to be significantly associated with this socio-demographic factor.

This table shows that residents with more than 100 work-hours per week are more at the "high" range of emotional exhaustion (90%) than those with 50-100 work-hours per week (76.2%), who are; in turn, more at the "high" range than residents working less than 50 hours a week (59.1%). The difference between the three groups is statistically insignificant.

The table also shows that residents with 50-100 work-hours per week are more at the "high" range of depersonalization (73.8%) than residents with more than 100 work-hours per week (50%), who are; in turn, more at the "high" range than those working less than 50 hours a week (45.4%). The difference between the three groups is statistically insignificant also.

A significant relationship between lack of personal accomplishment and the number of working-hours per week is proven in this table. Residents working less than 50 hours a week are more at the "high" range of lack of personal accomplishment (36.4%) than those with 50-100 work-hours per week (26.2%) who are; in turn, more at the "high" range than residents with more than 100 work-hours per week (20%).

At the same time, residents with more than 100 work-hours per week are more at the "low" range of lack of personal accomplishment (50%) than those with 50-100 work-hours per week (30.9%), who are; in turn, more at the "low" range than residents working less than 50 hours a week (27.3%).

Meanwhile, experiencing work-related stress associated with job setting and involvement with people is independent of work-hours per week.

Table (8) shows that residents with more than 100 work-hours per week are more at the "high" range of job setting-induced stress (60%) than those with 50-100 work-hours per week (42.9%), who are; in turn, more at the "high" range than residents working less than 50 hours a week (27.3%).

As regard to involvement with people, the residents with 50-100 work-hours per week are more at the "high" range of involvement with people-induced stress (38.1%) than those with more than 100 work-hours per week (30%), who are; in turn, more at the "high" range than residents working less than 50 hours a week (27.3%).

Sources of stress and burnout:

The different aspects of job setting have an upper hand over involvement with people as a source of stress among the resident physicians (Tables 9-10).

Low income and the imbalance between the effort and reward, together with the perception of the administration as being "poor" are the leading job setting stress-inducers of stress among the participants (Table 9).

A sense of helplessness toward the terminal patient and the mismatch of expectations between the patient (and his relatives) and physician are the major aspects of involvement with people that induce stress among the participants (Table 10).

The relationship between dimensions of burnout and sources of stress was strong and proven to be statistically significant (Table 11).

Work-induced emotional exhaustion (EE) proved to be significantly associated with job setting-induced stress experienced by participants (JS). However, depersonalization (DP) and lack of personal accomplishment (PA) are independent of this job setting-induced stress.

Table (11) shows a significant relationship between job setting-induced stress and emotional exhaustion, with all participants "highly" stressed by their job setting being at the "high" range of emotional exhaustion (100%).

However, this table shows that not only 75% of the study sample scoring "high" on the job setting-induced stress is being in the "high" range for depersonalization, but also 50% of those scoring "average" on the same dimension of sources of stress are in the "high" range for depersonalization. However, no statistical significant relationship has been found.

Also shown, about 22.2% of the study sample scoring "high" on the job setting-induced stress is being in the "high" range for lack of personal accomplishment. However, 31.2 % scoring "average" on the job setting-induced stress are in the "high" range for lack of personal accomplishment. This difference, however, has shown to be insignificant.

Work-induced emotional exhaustion, depersonalization, and lack of personal accomplishment prove to be dependent on involvement with people-induced stress (Tables 11).

The table proves a significant relationship between involvement with people-induced stress (IP) and emotional exhaustion (EE). Most of the participants scoring "high" on IP are in the "high" range for EE (89.3%). On the other hand, one-half of the participants in the "low" range for IP are in the "low" range for EE (50%).

This table proves a significant relationship between involvement with people-induced stress (IP) and work-induced depersonalization (DP). Most of the participants scoring "high" on IP are in the "high" range for DP (82.1%). As well, most of the participants in the "low" range for IP are in the "low" range for DP (60%).

Also, a significant relationship between involvement with people-induced stress (IP) and lack of personal accomplishment (PA) appears in this table. However, while 53.6% of the study sample in the "high" range of IP being in the "average" range of PA, only 39.3 % are in the "high" range for PA. On the other hand, most of the participants in the "low" range for IP are in the "low" range for PA (90%).

Table (1)

Item	Category	Number (Percentage) N=84
Gender	Male	64 (76.2)
	Female	20 (23.8)
Marital Status	Single	53 (63.1)
	Married	31 (36.9)
Work-Hour/Week	< 50	22 (26.2)
	50-100	42 (50)
	> 100	20 (23.8)

Table 2- Maslach Burnout Inventory subscale scores [mean ± SD] for the Participating residents:

Subscales	Participating Physicians	Normative Data Of Medical Practitioners
Emotional exhaustion (EE)	32.74 ± 10.49	22.19 ± 9.53
Depersonalization (DP)	14 ± 6.99	7.12 ± 5.22
Personal Accomplishment (PA)	35.03 ± 7.38	36.53 ± 7.34

Table 3- Number (Percentage) of Resident Physicians Scoring Low, Average and High on the MBI Subscales:

Subscale	Low	Average	High
Emotional exhaustion (EE)	≤16	17-26	≥27
Residents	6 (7.1)	15 (17.9)	63 (75)
Depersonalization (DP)	≤6	7-12	≥13
Residents	15 (17.9)	18 (21.4)	51 (60.7)
Personal Accomplishment (PA•)	≥39	38-32	≤31
Residents	29 (34.5)	32 (38.1)	23 (27.4)

•: PA is scored in opposite direction from EE and DP. Subjects scoring in the low category have high feelings of PA while those scoring in the high category have low feelings of PA

Table 4- Sources of Stress subscale scores [mean ± SD] for the participating residents:

Subscale	Participants
Job Setting (JS)	48.85 ± 10.51
Involvement with People (IP)	26.73 ± 8.39

Table 5- Number (Percentage) of Resident Physicians Scoring Low, Average and High on the SS Subscales:

Subscale	Low	Average	High
Job Setting (JS)	≤25	26-50	≥51
Residents	0 (0)	48 (57.1)	36 (42.9)
Involvement with People (IP)	≤15	16-30	≥31
Residents	10 (11.9)	46 (54.8)	28 (33.3)

Table (6) Gender perspectives associated with burnout and sources of stress:

	MaleN = 64		FemaleN = 20		P value
	No.	%	No.	%	
Relation between gender and EE					
LOW	5	7.8	1	5	P > 0.05
AVERAGE	11	17.2	4	20	
HIGH	48	75	15	75	
Relation between gender and DP					
LOW	11	17.2	4	20	P > 0.05
AVERAGE	13	20.3	5	25	
HIGH	40	62.5	11	55	
Relation between gender and PA					
LOW	23	35.9	6	30	P > 0.05
AVERAGE	23	35.9	9	45	
HIGH	18	28.2	5	25	
Relation between gender and JS					
LOW	0	0	0	0	P > 0.05
AVERAGE	39	60.9	9	45	
HIGH	25	39.1	11	55	
Relation between gender and IP					
LOW	10	15.6	0	0	P > 0.05
AVERAGE	35	54.7	11	55	
HIGH	19	29.7	9	45	

Table (7) Relationship between marital status and dimensions of burnout and sources of stress:

	Single N = 53		Married N = 31		P value
	No.	%	No.	%	
Relation between marital status and EE					
LOW	5	9.4	1	3.2	P > 0.05
AVERAGE	11	20.8	4	12.9	
HIGH	37	69.8	26	83.9	
Relation between marital status and DP					
LOW	10	18.8	5	16.1	P > 0.05
AVERAGE	13	24.5	5	16.1	
HIGH	30	56.6	21	67.8	
Relation between marital status and PA					
LOW	23	43.4	6	19.4	P < 0.05
AVERAGE	15	28.3	17	54.8	
HIGH	15	28.3	8	25.8	
Relation between marital status and JS					
LOW	0	0	0	0	P > 0.05
AVERAGE	30	56.6	18	58.1	
HIGH	23	43.4	13	41.9	
Relation between marital status and IP					
LOW	8	15.2	2	6.4	P > 0.05
AVERAGE	27	50.9	19	61.3	
HIGH	18	33.9	10	32.3	

Table (8) Relationship between work-hours/week and the dimensions of burnout and sources of stress:

	< 50 N = 22		50 – 100 N = 42		> 50 N = 20		P value
	No.	%	No.	%	No.	%	
Relation between work-hours/week and EE							
LOW	4	18.2	1	2.4	1	5	P > 0.05
AVERAGE	5	22.7	9	21.4	1	5	
HIGH	13	59.1	32	76.2	18	90	
Relation between work-hours/week and DP							
LOW	6	27.3	6	14.3	3	15	P > 0.05
AVERAGE	6	27.3	5	11.9	7	35	
HIGH	10	45.4	31	73.8	10	50	

Table (8): **continue**:

	< 50 N = 22		50 – 100 N = 42		> 50 N = 20		P value
	No.	%	No.	%	No.	%	
Relation between work-hours/week and PA							
LOW	6	27.3	13	30.9	10	50	P < 0.05
AVERAGE	8	36.4	18	42.9	6	30	
HIGH	8	36.4	11	26.2	4	20	
Relation between work-hours/week and JS							
LOW	0	0	0	0	0	0	P > 0.05
AVERAGE	16	72.7	24	57.1	8	40	
HIGH	6	27.3	18	42.9	12	60	
Relation between work-hours/week and IP							
LOW	4	18.2	5	11.9	1	5	P > 0.05
AVERAGE	12	54.5	21	50	13	65	
HIGH	6	27.3	16	38.1	6	30	

Table 9- Aspects of Job setting experienced by Participants causing extreme stress:

Aspect	No.	%
Gaining less money for doing more	66	78.6
A sense of poor organization and loss of contact with administration	64	76.2
Negative feedback predominates, while positive feedback is minimal	57	67.9
No time to follow up-to-date medical literature	56	66.7
Long working hours with no enough breaks for rest	48	57.1

Table 10- Aspects of Involvement with People experienced by Participants causing extreme stress:

Aspect	No.	%
Inability to induce a change or improvement with terminal cases	48	57.1
Mismatch of expectations between patient and physician	42	50
Inability to empathize with certain patients (esp. the recommended ones)	41	48.8
Lack of positive feedback about patient's improvement after discharge	38	45.2
Lack of appreciation and a lot of blame from patients and their families	36	42.9

Table (11) Relationship between burnout and sources of stress:

JS / EE	Low N=0		Average N=48		High N=36	
	No.	%	No.	%	No.	%
Low	0	0	6	12.5	0	0
Average	0	0	15	31.3	0	0
High	0	0	27	56.2	36	100
P value < 0.05						
JS / DP	Low N=0		Average N=48		High N=36	
	No.	%	No.	%	No.	%
Low	0	0	10	20.8	5	13.9
Average	0	0	14	29.2	4	11.1
High	0	0	24	50	27	75
P value > 0.05						
JS / PA	Low N=0		Average N=48		High N=36	
	No.	%	No.	%	No.	%
Low	0	0	19	39.5	10	27.8
Average	0	0	14	29.2	18	50
High	0	0	15	31.3	8	22.2
P value > 0.05						
IP / EE	Low N=10		Average N=46		High N=28	
	No.	%	No.	%	No.	%
Low	5	50	1	2.2	0	0
Average	2	20	10	21.7	3	10.7
High	3	30	35	76.1	25	89.3
P value < 0.05						
IP / DP	Low N=10		Average N=46		High N=28	
	No.	%	No.	%	No.	%
Low	6	60	8	17.4	1	3.6
Average	4	40	10	21.7	4	14.3
High	0	0	28	60.9	23	82.1
P value < 0.05						
IP / PA	Low N=10		Average N=46		High N=28	
	No.	%	No.	%	No.	%
Low	9	90	18	39.2	2	7.1
Average	0	0	17	36.9	15	53.6
High	1	10	11	23.9	11	39.3
P value < 0.05						

Discussion:

Burnout seems to be prevalent and severe among residents of the study sample. The reasons for such high levels of burnout among new medical graduates are likely to be complex, and to reflect both the environment in which young doctors work and personal characteristics of the doctors themselves (Firth-Cozens, 1987), and cannot be attributed to single issues such as working hours (Firth-Cozens & Moss, 1998).

More than 63% of the study sample suffers from burnout using the criteria of scoring ”high” in at least two of the three dimensions of burnout; with considerably high mean scores for emotional exhaustion, depersonalization and lack of personal accomplishment. This is especially dangerous as the presence of any combination of the features of burnout leads to decreased effectiveness at work (Maslach et al, 1996). Not only that, but also resident burnout could contribute to the dehumanizing effects of medical education—especially for medical students, and for other residents as well.

Socialization of medical students has been described as a “hidden curriculum” in which students acquire attitudes and habits from other physicians, (Hafferty & Franks, 1994). The high rate of burnout among residents, who spend far more time with medical students (Barnett et al, 1999) and each other than with faculty physicians, raises the possibility that resident burnout influences what medical students and junior residents interpret as appropriate professional behavior. Burnout could contribute to increases in cynicism and decreases in compassion that have been observed over the course of postgraduate training (Colford & McPhee, 1989).

Rates of emotional exhaustion and depersonalization rise significantly during the residency years (Willcock et al, 2004). If the non-respondents in this study were taken into consideration (32 physicians), the prevalence may have ranged from 46% (if all were not burnt out) to 73.6% (if all were). Shanafelt et al (2002) found that burnout was very common among residents in all 3 years of residency training: More than 75% of respondents in his study met the criteria for burnout. If it means anything, it is the burden of residency on the young physicians.

In terms of personal impact of work-related stress, work-induced emotional exhaustion was identified in 75% 0f participant residents, depersonalization in 60.7%, and lack of personal accomplishment in 27.4%; figures that are remarkably higher than what Velamoor et al (2000) found in the study carried out on a sample including senior as well as junior physicians (32.4%, 10.3%, 13.1% respectively).

However, burnout; as shown from this study is neither a reflection of the physician’s socio-demographic characteristics, nor a matter of prolonged hours of working. There were no significant differences between perceived stress levels in the males and females on direct comparison, which is similar to what Rathod et al (2000) found in their study of burnout. It is suggested that women have lower job expectations than men, are socialized not to express discontent, and value different characteristics in a career than do men (Phelan, 1994); characteristics that might recommend women to be less stressed by their job settings and interactions with people. However, in the current study sample, women are found

more at the "high" ranges of work-induced stress, an observation that may reflect cultural discrepancies between women from the two studies.

Work-induced emotional exhaustion, depersonalization, and lack of personal accomplishment were independent of the socio-demographic factors of sex or marital status; something repeatedly proved by Velamoor and his colleagues (2000). A survey conducted in the Netherlands surveying 1426 physicians in primary care and specialties (response rate, 63%; 18% women), the authors found no significant sex difference in burnout rates in Dutch physicians (Linzer et al, 2002). The power of physicians, defined as a combination of clinical freedom, autonomy, authority, influence, and participation in decision-making, has been decreasing both among male and female physicians (Friedman, 1995; Forsberg et al, 2001). The findings of no significant differences on any of the socio-demographic factors for the personal impact of work-related stress suggest equal vulnerability to emotional exhaustion, depersonalization, and lack of personal achievement.

Only "lack of personal accomplishment" proved to be influenced by socio-demographic factors. Single participants seem to be more into their job and more extreme in their attitude toward their accomplishment than their married colleagues, who may have other sources for a sense of accomplishment that their single counterparts do not have. Also, residents appear to get their sense of personal accomplishment from the number of hours they work- the more the hours the more the accomplishment. Such an attitude can reflect the way in which residents are being evaluated and the major aim they seek during their residency, namely; their seniors' appreciation. Although residents complain about the long working hours they have to admit to, they consider the number of working hours as the main evaluative tool for their accomplishment. This is not all good though, because it is the quality; not the quantity, that matters in medical practice.

On the other hand, burnout is more a matter of what the resident has to deal with in his or her workplace; namely the job setting and involvement with people. As it might appear in the current study, work-induced burnout proved to be dependent on work-induced stress. In 2001, Richard Smith asked "Why are doctors so unhappy?" and concluded that "The most obvious cause of doctors' unhappiness is that they feel overworked and under-supported" (Smith, 2001). As well, professional unhappiness among physicians, with increasing stress and decreased well-being, might partly be due to worsening working conditions (von Vultée et al, 2004).

However, some aspects are more stressful than others. Poor financial gain, poor contact with administration and negative feedback from seniors are especially stressful job settings, while a sense of helplessness toward terminal cases ranked first in the stressful aspects of involvement with people. This is at the time when it is known that: as a buffer against work-related stress, the support, which junior staffs perceive from consultants, may be crucial (Firth-Cozens, 1987).

Mismatch between the expectations of the patient and physician is another aspect of involvement with people-induced stress. This is especially true as the process of burnout "exhausts one's physical and mental resources by excessively striving to

reach some unrealistic expectation imposed by oneself or by the values of society" (Wessels et al, 1989).

Other common themes that are worthy of consideration seem to emerge from the findings on appraisals of work-related stress among medical faculty include: non-clinical functions (excessive paperwork), dealing with difficult patients, and dealing with relatives of patients (Velamoor et al, 2000). In another study, the areas most frequently rated as stressful were: out of hours duties, dealing with difficult and hostile relatives of patients, working long hours, arranging admissions, paperwork, demands of job interfering with personal life, and responsibility of suicidal and homicidal patients on increasing workload and bed scarcities (Rathod et al, 2000).

It has been stated "The attitude of the medical profession to the health of its members has always been one of disinterest which is transiently discarded when disaster overtakes one of its members ('Hagan & Richards, 1998).

It is incumbent on the individuals and healthcare systems that employ and supervise the new generation of medical practitioners that these young doctors are given the same care and support that people expects them to provide to their patients (Willcock et al, 2004).

The current study had several important limitations. Although the response rate was high, response bias remains a possibility, and the prevalence of burnout in this residency program could range from 45%, if all 32 non-respondents were not burned out, to 73.7%, if all non-respondents were burned out.

It was not possible to compare respondents with non-respondents because, to fully protect the anonymity of all residents (regardless of participation); we obtained only limited demographic information from respondents.

The outcome measures for work-induced stress were based on self-report, and it is not possible to know the extent to which these self-reports accurately reflect the degree of stress caused by the different aspects of job setting and involvement with people assessed in the survey. Criterion validity and reproducibility of the questions have not been studied. In addition, biased reporting of work-induced stress could explain the observed relationship between burnout and stress experienced due to job setting and involvement with people. For example, residents who met criteria for burnout could have over-reported work-induced stress they experience. Alternatively, residents who were not burned out might have been more susceptible to social desirability bias; therefore, these residents could have under-reported their work-induced stress.

Although the author believes the results regarding the association between burnout and work-induced stress should be viewed cautiously and should be used primarily to generate hypotheses for future research, the author doubts that these findings solely reflect biased reporting. Finally, this study is limited by its cross-sectional design. Future longitudinal studies are required to evaluate the possibility of a causal relationship between work-induced stress and burnout.

The generalizability of the results in this sample of residents from a single university hospital is unknown. However, the author doubts that the results reflect unique characteristics of the residency program or residents studied, as residents in this

hospital work in inpatient and outpatient settings that are typical for Egyptian university-based training programs in different specialties. For this reasons, it seems unlikely that these findings are unique to the hospital that was studied.

Recommendations:

Annual self-assessment of the level of burnout and work-induced stress, using validated measuring tools (e.g. MBI), to follow-up the level of burnout among the residents.

Establishing a mechanism for providing psychiatric counseling for physicians identified as "burned out" through the Psychiatry Department.

Organizing regular meetings between residents on one side and administration members and patients' relatives on the other side to simplify and clarify various controversies and to communicate openly.

Strict regulations considering the number of hours the resident has to work per week, which – if violated- give the resident the right to get more "off" hours.

Workshops for junior residents about the essential social skills they may need in dealing with different personalities

Improving the financial reward the residents gain from their work in respect to the duties they have to attain.

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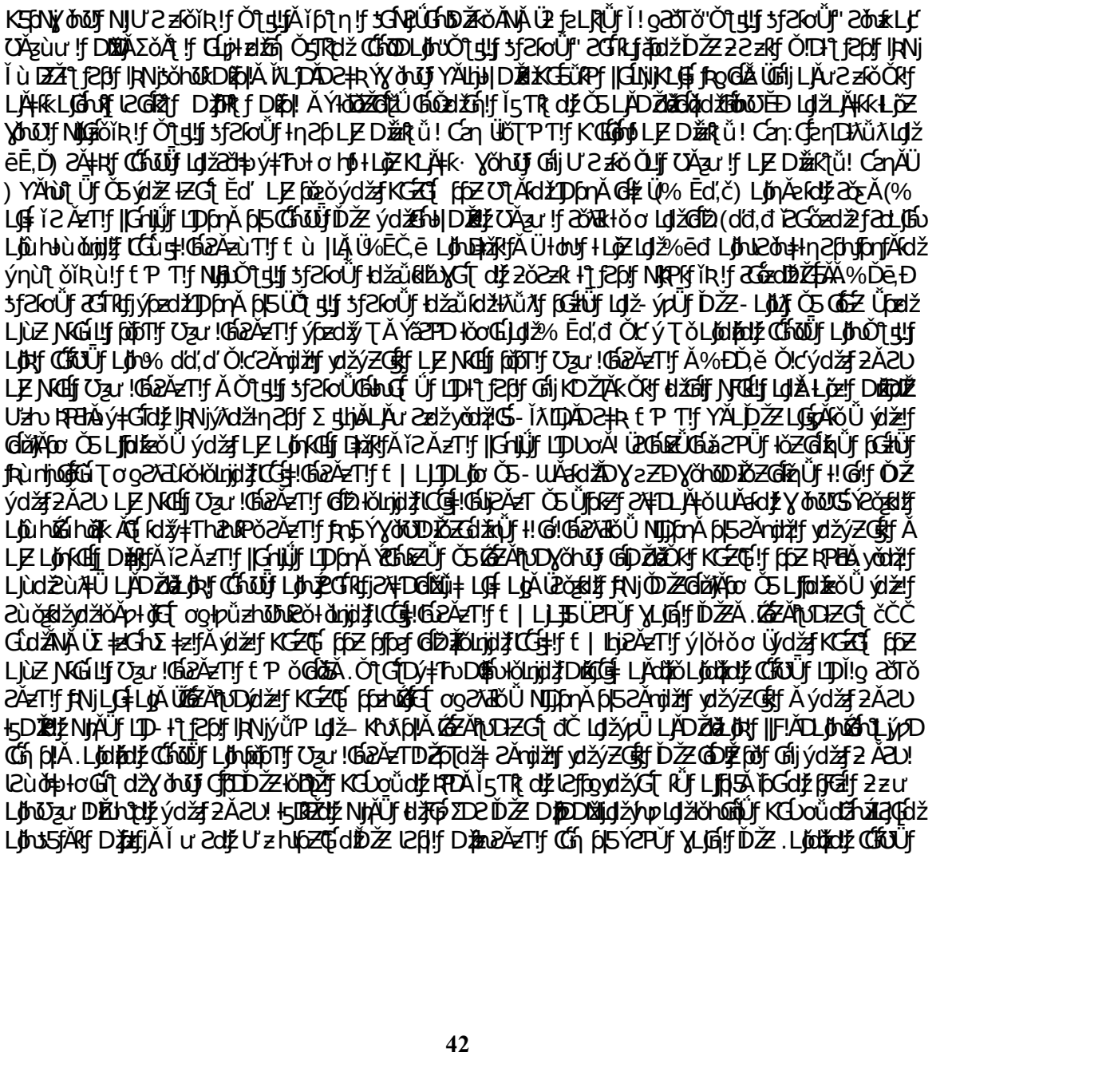
متلازمة الاحتراق النفسي بين الأطباء المقيمين في مستشفي جامعة قناة السويس



Amphetamine Related Symptoms: Descriptive Analysis and Reasoning

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Abstract

At the last few years a lot of data in the gulf region reported that amphetamine psychosis became more common and more prolongedThis study was done to: 1) assess clinical features related to amphetamine withdrawal, 2) assess if there are changes in these features in comparison to other previous studies or not, 3) study the relation between amphetamine and chronicity of psychotic symptoms, 4) Find a reason for such suspected changes if present. A total of 150 male amphetamine dependent inpatient were selected according to ICD-10 research diagnostic criteria. Patients were subjected to the following procedures: 1) Oral informed consent. 2) Full psychiatric interview. 3) Urine test for common addictive substances on admission 4) Symptoms checklist which have been designed by the authors to assess Clinical features associated with amphetamine 5) Symptom Checklist–90—Revised (Derogates 1994). Generally the present study shows that the psychotic symptoms were very common with Amphetamine dependent patients and the severity of all symptoms decreased significantly during the different phases of treatment. Delusions and hallucinations were very common during 2nd week (54% and 51% respectively) and persisted for more than 8 weeks in 24% and 10% of patients respectively. 1999 and Koyama et al 1991 but still the duration of psychosis is much longer. There is increased risk of psychosis with use of amphetamine and a lot of reasons may play role as starting abuse at early age, sensitization process that may lead to chronic psychosis, and adulterating substances like ephedrine that may be dangerous and can lead to permanent damage of brain serotonin nerve endings.

Introduction

Drug dependence is a chronic problem in all countries of the world. The prevalence of Drug abuse and addiction continue to be among the largest and most challenging health, economical, ethical and social problems facing society.

Many studies raised great concern about the prevalence of amphetamine dependence and its associated problems especially psychosis ***(Farrel et al 2002, Dalamu et al, 1999, Muray, 1998 and Koyama et al, 1991).***

The classic amphetamines have their primary effects by causing the release of catecholamine particularly dopamine from presynaptic terminals. The effects are particularly potent for the dopaminergic neurons that project from the ventral tegmental area to the cerebral cortex and the limbic areas. That pathway has been termed the rewarding pathway and its activation is probably the major addicting mechanism for the amphetamines. Amphetamine induced psychosis has been extensively studied because of its close resemblance to paranoid schizophrenia. Several studies have also found that, although the positive symptoms of schizophrenia and amphetamine induced psychosis are similar, the affective flattening of schizophrenia and also alogia are generally absent in amphetamine induced psychotic disorder. Clinically, however, acute amphetamine induced

psychotic disorder can be indistinguishable from schizophrenia and only the resolution of the symptoms in a few days or a positive finding in a urine drug screening test eventually reveals the correct diagnosis.

Some evidence indicates that the long term use of amphetamines is associated with an increased vulnerability to the development of psychosis under a number of circumstances including alcohol intoxication and stress. Previous studies reported that psychotic symptoms only develop after prolonged use and typically at high doses and usually only hours in length and maximum for few days ***(Kaplan and Sadock, 2000).*** However at the last few years a lot of data in the gulf region reported that amphetamine psychosis became more common and more prolonged.

Patients admitted to Al-Amal complex are subjected to a preset program as patients are received in a detox unit for few days till they recover from physical withdrawal symptoms and/or psychotic symptoms then patients are transferred to rehabilitation units to receive other modalities of therapies. In the last few years it was noticed that the mean duration of stay in detox units was increasing. Also, cases of amphetamine dependence increased gradually along these years (***annual Report 2005, Alamal complex***). These observations has led the authors to investigate symptoms related to amphetamine especially psychotic features.

Aim

This study was done to: 1) Assess clinical features related to amphetamine withdrawal. 2) Assess if there are changes in these features in comparison to other previous studies or not. 3) Study the relation between amphetamine and chronicity of psychotic symptoms. 4) Find a reason for such suspected changes if present.

Methods

This study was done in Al-Amal Complex for mental health which is located in Al-Dammam, Kingdom of Saudia Arabia (KSA). It is a 500 bed hospital, 200 for addiction, 150 bed for half way house for abstinent patients and 150 bed for psychiatric patients. The complex serves all the Eastern and Northern provinces of KSA in addition to nearby other gulf countries like Bahrain, Kuwait, Doha, etc. yearly the Addiction treatment in patient units in this complex dealt with more than 2000 case. At the last three years patients dependent on amphetamine only constitute more than 50% of patients dependent on one substance ***(Al-Amal complex annual report 2005)***

A total of 150 male amphetamine dependent inpatient at Al Amal Mental Health complex were selected according to ICD-10 research diagnostic criteria (during a period of 8 months. Cases who reported any significant history of other substances use within past two years or who had a previous history of a major psychiatric disorder not related to amphetamine were excluded. After start of the study 19 cases were excluded after getting data from their informants about history of previous depression, schizophrenia, mania and use of other substances.

All patients subjected to the following procedures: 1) Oral informed consent to take part in the study. 2) Complete psychiatric interview. 3) Urine test for common addictive substances on admission to confirm the diagnosis of amphetamine use without any other substances. 4) Symptoms checklist which have been

designed by the authors to assess Clinical features associated with amphetamine. It was applied daily from the first day of admission till the second week then weekly till discharge. 5) Symptom Checklist–90—Revised (SCL-90-R) (Derogates 1994) which is a quick screening instrument, to measure the status of psychopathology, and as a quantification of current psychopathology along nine symptom constructs: Somatization, Obsessive-Compulsive, Interpersonal Sensitivity, Depression , Anxiety, Hostility, Phobic-Anxiety Paranoid Ideation , and Psychoticism. It is a self-administrated questionnaire. Instructions direct respondents to report how much discomfort each item caused them during the previous weeks. Items are numbered rejoinders to the opening stem "How much were you distressed by . . . ?" Respondents mark one numbered circle for each item on a Liker t-type scale of 0 = not at all, 1 = a little bit, 2 = moderately, 3 = quite a bit، and 4 = extremely. SCL-90 6) Each patient was asked specifically during the interview about, starting age of abuse of amphetamine, duration of abuse, dose, number of previous hospitalizations and past history of psychosis related to use of amphetamine. 7) In addition to the procedures done for patients, 7 different types of amphetamine tablets available in the market were collected through narcotic prevention department and the content of such types were analyzed through the central toxicology laboratory in Dammam central Hospital by expert professor of chemistry and toxicology.

Only data of 131 patients were subjected to the statistical analysis. The symptoms checklists results were collected and statistically analyzed utilizing mean, standard deviation, and frequencies, discriminate function analysis, to compare the daily differences. All collected data were Statistical analyzed using SPSS version 12 (2003). All given percentages are approximated numbers done by the computer.

Results

The Mean age of the patients included in the sample was 26.24 SD± 5.4. Regarding the demographic data of this sample, 76 % were currently single, 14 % were married, and 8% divorced, 2% widows. Regarding Educational level 51% were graduated from Middle school, 22% Primary school ,11% Secondary school, 6% illiterate and 4 % can read and write, while there were 6% University graduates. In regard of the Place of residence, 78% were from eastern province, 7% from western province, 5% from south and 4% from north province and 6% from other nearby Gulf countries. The results of urine toxicology showed that 42% had negative results, where 58% had positive results on admission .the samples were collected on the second day of admission. Regarding the family history of substance use, the majority of that sample 82% had negative results and 18% had positive results. Although no personality tests were administred on our patients, the results of clinical evaluation revealed that 22 % were diagnosed as having personality disorder.

Tables 1: the common symptoms of the Amphetamine patients in the first and 2nd weeks

Symptoms	Frequency(first week)		Frequency(second week)	
Objective symptoms (Physical)	**Normal**	**high**	**Normal**	**high**
Blood pressure	%96	%4	%98	%2
Sweating	%64	%36	%20	%80
Tachycardia	%84	%16	%90	%10
Vomiting	%90	%10	%100	%0
Diarrhea	%94	%6	%100	%0
Sneezing	%88	%12	%100	%0
Sleep disorder	%42	%58	%42	%31
Dilated pupils	%90	%10	%100	%0
Tremors	%82	%18	%100	%0
Back pain	%90	%10	%100	%0
Running nose	%86	%14	%100	%0
Fever	%96	%4	%100	%0
Subjective symptoms (Psychological)				
Headache	%76	%24	%98	%2
Delusions	%72	%28	%46	%54
Hallucinations	39%	61%	49%	51%
Chest tightness	%89	%12	%98	%2
Anxiety	%56	%44	%57	%43
Abdominal pain	%98	%2	%100	%0
Restless	%66	%34	71%	29%
Depressed mood	%54	%46	%62	%38
Irritability	%58	%42	%88	%12
Abnormal behavior	%68	%32	%12	%88

Tables 2: the common symptoms of the Amphetamine patients in the 3rd and 4th weeks

Symptoms	Frequency(3rd week)		Frequency(4th week)	
Objective symptoms (Physical)	Normal	high	Normal	high
Blood pressure	%97	%3	%99	%1
Sweating	%81	%19	%88	%12
Tachycardia	%92	%8	%94	%6
Vomiting	%100	%0	%100	%0
Diarrhea	%99	%1	%100	%0
Sneezing	%99	%1	%100	%0
Sleep disorder	%73	%27	%77	%23
Dilated pupils	%100	%0	%100	%0
Tremors	%100	%0	%100	%0
Back pain	%99	%1	%100	%0
Running nose	%98	%2	%100	%0
Fever	%100	%0	%100	%0
Subjective symptoms (Psychological)				
Headache	%97	%3	%96	%4
Delusions	%55	%45	%61	%39
Hallucinations	68%	32%	79%	21%
Chest tightness	%95	%5	%97	%3
Anxiety	%51	%49	%71	%29
Restless	79%	%21	%76	%24
Depressed mood	%65	%35	%77	%23
Irritability	%90	%10	%96	%4
Abnormal behavior	%68	%32	%69	%21

Generally the present study shows that physical symptoms were mild and un common with Amphetamine withdrawal and the severity of symptoms decreased significantly within short time. The physical withdrawal symptoms generally peak in 2 to 4 days and are resolved in most of cases within first week. The most common physical withdrawal symptoms were excessive sleep and sweating while the most serious physical withdrawal symptom was tachycardia (16% in first week).

The most common psychological withdrawal symptoms were delusions, hallucinations, depressed mood and anxiety symptoms. The most serious psychological withdrawal symptom was depression that can be severe after sustained use of high doses and can be associated with suicidal ideation or behavior. Psychological withdrawal symptoms started during the first week and in some cases persisted for more than 8 weeks. Percentage of cases had delusions increased during the second week and decreased gradually during the following weeks.

84% of cases reported a previous history of psychotic symptoms associated with use of amphetamine. 34% of the sample reported that they had used amphetamine on over 100 separate occasions. Those frequent users were at greater risk of psychosis than those who had used less extensively. For those who had used amphetamine on over 100 occasions, the risk of delusions was more than double that of other users (OR=2.37, $P < 0.01$).

Starting use of amphetamine before the age of 18 years also doubled the risk of developing delusions odd ratio = 2.73, $P<0.05$. Early amphetamine use before age of 18 years has been also, associated also with multiple hospitalizations.

Also, there was positive correlation between presence of delusions and history of previous psychosis, number of previous hospitalizations, duration of stay n the hospital and daily dose of amphetamine.

Tables 3: the mean Score on SCL-90 R of the Amphetamine patients.

Scale Items	Mean	SD
Somatization	.43	.32
Obsessive-compulsive	.97	.81
Interpersonal Sensitivity	1.69	.33
Depression	1.23	.67
Anxiety	1.12	.39
Hostility	1.20	.42
Phobic- anxiety	.80	.22
Paranoid ideation	1.48	.47
Psychoticism	1.01	.32

The results showed that there were high scores of Interpersonal Sensitivity, hostility due to suspiciousness, delusion of persecutions, Paranoid ideation, and Psychoticism. In the other side, the depression was also higher than average level.

Duration of hospitalization was 4-5 weeks in 21% of cases, 5-6 weeks in 34%, 6-8 weeks in 30%, and 15% more than 8 weeks. At discharge 24% of patients still have delusions and 10% still have hallucinations.

Analysis of the amphetamine tablets revealed that each tablet contain different amounts from different substances even if it is from the same type (same the shape and color). Some of the tablets analyzed have no amphetamine at all. Ephedrine and pseudoephedrine were common finding in most of tablets analyzed. Other substances like caffeine, theophylline, diphenhydramine, methyle salicylates, quinine and ascorbic acid were also found.

Discussion

Previous studies denoted that typically symptoms of amphetamine psychosis remit within a week, but in a small proportion of patients, psychosis may last for more than a month ***(Kaplan and Sadock, 2000; Koyama et al , 1991; and Kandel and Davis 1996)***. Some amphetamine users may develop persistent psychosis and those who recover remain at high risk of reexperiencing psychosis even if they don't use amphetamines again ***(Hyman and Nesteler, 1996; and Farrel et al 2000)***

Although Amphetamine dependent patients are usually of a younger age ***(Battaglia and Napier, 1998),*** the results showed that there are no cases below 18 years (Mean age of 26.24 SD$\pm$ 5.4), Because of the admission policy of Al-Amal mental complex, which does not permit admission below this age. Regarding the educational level of our sample, only 6% was university graduated, which could be explained on basis of level of education and more maturity. The Middle school graduated represented the highest percentage of the sample because at this level of education they sought to work in governmental places, and some of them are referred from their work for assessment and management. Regarding marital status the results showed that 86% the sample were singles probably due to social stigma of addiction, and unemployment.

As regards to the physical withdrawal symptoms, all results were concordant with results of previous studies ***(Dalamu et al 1999 and Koyama et al 1991)*** which denoted that most of physical symptoms disappeared during the first week and that the most resistant objective symptoms are sleep disorders and sweating **(Iwanami, et al 1994)** . Sleep disorders are explained by the powerful effect of the amphetamine as a stimulant on reticular activating system while the prolonged sweating is explained by the tendency of autonomic disturbance to persist more and to adapt more slowly than other body systems ***(Kaplan and Sadock, 2000).***

Patients were examined daily by symptom checklist and to avoid biased judgment from patients and clinician themselves application of SCL-90 R was done weekly. High scores of Interpersonal Sensitivity, hostility, delusion of persecutions, Paranoid ideation, depression and psychoticism confirmed the clinical assessment done and gave an objective score. Delusions and hallucinations were more common in the second week than in the first week as patients are more distressed by physical

symptoms and increased sleep during first week and when they start to communicate these psychotic features started to appear more prominently.

Persistent mood symptoms like depressed mood for more than 4 weeks in 23% of cases is concordant with other studies ***(Koyama et al 1991 and Murray 1998)*** as amphetamine is powerful stimulant for dopamine and its ingestion for long periods will be followed by dysregulation of dopamine receptors and readjustment of these receptors after withdrawal will take time because it is a structural brain change ***(Farrel et al 1998).***

Persistent delusions, hallucinations, and abnormal behaviors for 4 weeks in 39%, 31% and 29% of cases respectively confirmed the clinical observation noticed empirically. Previous studies about duration of psychotic symptoms denoted that only 15% of patients persisted to be psychotic at the 4th week ***(Brabbins and Poole, 1996, Brady et al, 1991, and Satu et al, 1990).*** The argument that the subjects found in this study are not suffering from psychosis but simply manifesting the toxic effects of amphetamine has been examined and excluded because toxic effects by definition in ICD-10 research diagnostic criteria don't exceed 48 hours. ICD-10 Classifications permitted for psychosis to appear within two weeks from taking the substance and to last at least more than 48 hours and at most 6 months ***(WHO, 1992)*** but there is idea about the commonest duration of psychosis as classifications addressed other issues like medicolegal aspects

This persistence of psychotic symptoms can be attributed to the change in structure of amphetamine tablets as analysis of tablets revealed wide use of ephedrine as an additive and it is well known in the literature that this substance can lead to permanent damage of brain serotonin nerve endings that have a major role in psychosis and depression ***(Ellenhorn, et al, 1990)***. The second major cause for persistence of psychotic symptoms was the kindling process ***(Kaplan and Sadok, 2000)*** as denoted by The positive correlation between early use of amphetamine before age 18 years, duration of use of amphetamine, dose, number of hospitalizations. Where as dopamine neurotransmission is increased in response to a single dose of amphetamine and this would suggest that repeated increases in dopamine release may produce secondary changes that are more directly responsible for the persistence of psychosis ***(Cherland and Fitzpatrick, 1999 and Farrel et al 1998).***

Another possible interpretation of persistence of psychotic features with amphetamine is that individual with predisposition to psychosis are more likely to use drugs and drugs work as precipitating factor not an inducing factor. But this interpretation can be minimizd by the fact that drug induced psychosis is not common with other substance like opiates or benzodiazepines as with amphetamine ***(Peroutka , 1988 and Murray 1998)***

Reports from narcotic prevention department revealed that most of amphetamine was imported from outside the country in the past but at the last few years there is local synthetic amphetamine and this interpretate the different structure of different types of amphetamines and interpret adulteration with many things like salicylic acid , antihistaminincs, quinine and the most dangerous was ephedrine.

Conclusion

It is misleading and dangerous, to our youth in particular, to label Amphetamine as "soft drug" and to be socially accepted. In fact the serious adverse effects of Amphetamine let it as one of the worst substances in our countries.

Policy implications

Severe dependence on amphetamine was associated with higher risk of psychosis so services should be directed more toward this type of addiction especially that current services are more directed toward substances like heroin.

Opening of special units for drug induced psychosis will be beneficial because those cases block detox units and will disturb rehabilitation units. This research help to stress that the plan of narcotics prevention should be adapted and modified to restrict local synthesis of these substances.

Clinical implications

This work reflects the importance of clinical observation to monitor changes in the presentation of patients. Also it reflects the importance of integrating clinical observation with chemical assessment of the available illicit drugs

Following recovery persons who have experienced an amphetamine-induced psychosis seem to be sensitized and will experience acute paranoid psychosis on reexposure to small doses of amphetamines.

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Sleep Profile in Children with Pervasive Developmental Disorders

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Abstract

Sleep disturbances are regarded as a common clinical feature in autism and other Pervasive Developmental Disorders (PDD) that forms a great source of stress for families. Studies have shown that children with PDD exhibited qualitatively and quantitatively different sleep patterns to non autistic control children. This study aimed at describing sleep patterns in a sample of Egyptian children with pervasive developmental disorders. The study included 15 children with a pervasive developmental disorder according to DSM-IV criteria, randomly chosen from the child psychiatry out patient clinic, at the Institute of Psychiatry, Ain Shams University between the months of January and August, 2004. An age and sex matched control group, formed of 10 healthy age and sex matched children from the information bank of the sleep laboratory were obtained. All cases were clinically assessed and the severity of the PDD was further evaluated by the Childhood Autism Rating Scale (CARS). Subjective sleep assessment was obtained through the Arabic version of Children's Sleep Habits Questionnaire (CSHQ). Sleep was also objectively assessed by a polysomnogram performed at the sleep lab of the institute of psychiatry, Ain shams University. The children were classified as mildly autistic or moderately autistic by the CARS. Epilepsy was reported in 46.7% of the patients. Normal sleep latency was reported in 60% of the patients while 26.7% reported a moderate increase in sleep latency. The children's sleep habits questionnaire (CSHQ) showed that sleep duration was adequate in 93.3% of patients. Sleep related anxiety was seen in 53.3% of patients and night awakening in 40% of patients. Nocturnal enuresis was seen in 20% of patients (3 patients) and increased movements during sleep in 26.7% (4 patients). Sleep bruxism was seen in 20% of patients (3 patients), while sleep disordered breathing occurred in one patient. As compared to age and sex matched control, the polysomnogram has shown a significant decrease in sleep efficiency, prolongation of stage 1 and 2 NREM sleep and shortened REM sleep in patients with PDD. The arousal index and number of awakenings were significantly higher in children with PDD than in the control group. The Periodic Leg Movements during Sleep index was also significantly higher in the patient than the control group. The results of our study confirm the presence of sleep disturbances in children with PDD in the form of decreased sleep efficiency and change of sleep

Introduction:

The pervasive developmental disorders (PDD) are a group of disorders in which the main features are delay and deviance in the development of social skills, language and communication, and limited and stereotyped repertoire of behavior and interests. Autism is the prototype of these disorders but the group also includes Asperger syndrome, childhood disintegrative disorder, Rett syndrome and PDD not otherwise specified (Kaplan and Sadock, 1998). The differentiation between these disorders is mainly behavioral with no structural, biochemical or etiological factor identified as specific to any PDD subtype (Willemson-Swinkels and Buitelaar, 2002). The exact causes underlying these disorders are not fully understood but it is believed to

be heterogeneous, with interactions between genetic and environmental factors. A variety of disorders were associated with autism including viral infections, inborn errors of metabolism, structural lesions of the brain, congenital or early neonatal infections, suboptimal obstetric conditions, disturbed absorption from the gastrointestinal tract, altered immunological reactions and endocrinal disturbances. All these factors are believed to act through a final common pathway to affect development of the brain at a critical period resulting in the behavioral syndrome that we call autism (Gilberg and Coleman 2000).

Sleep disturbances are regarded as a common clinical feature in autism and other PDD that forms a great source of stress for families (Herring et al., 1999). Studies have shown that children with PDD exhibited qualitatively and quantitatively different sleep patterns to non autistic control children (Patzold et al., 1998). Villalba and co-workers (2002) classified disorders of sleep in infantile autism into three types:

A) Functional alterations in sleep; with early waking and difficulties in going to sleep being the disorders most frequently seen.

B) Immaturity of sleep: showing a disturbed polysomnographic recording and negative correlations with the level of development.

C) Paroxysmal alterations: with epileptiform discharges being the commonest, without necessarily occurring with seizures.

The exact causes of these sleep disturbances is not fully understood. A variety of factors are believed to play a role including difficulties to regulate sleep and wake cycles according to social clues, altered sensory perception with increased sensitivity to minor environmental changes and increased levels of anxiety (Richdale and Prior, 1995; Patzold et al., 1998). Sleep disturbances may also reflect functional alterations in the neurological structures responsible for regulation of the sleep–wake cycle, and may reflect abnormalities in brain maturation and neurotransmitter systems (Richdale, 1999).

Sleep problems have been correlated with increased personal and family distress and is believed to adversely affect daytime behavior (Patzold et al., 1998) including increased rates of over activity, disruptive behavior, communication difficulties and stereotyped behavior (Patzold et al., 1998; Schreck et al., 2004). Only a few studies have investigated sleep disorders in children with autism and most of these were based on parental reports through sleep diaries or sleep questionnaires. The issue of the objectivity of parental reports was put forth as a potential weakness in various studies. The difficulty inherent in studying autistic children who are intolerant to changes in routine or environment is a likely reason for the paucity of nocturnal polysomnographic studies, even in symptomatic children with an obvious sleep disturbance (Thermulai et al., 2002).

This study aimed at describing sleep patterns in a sample of Egyptian children with pervasive developmental disorders. Children were assessed by means of a clinical history and Childhood Autism Rating Scale (CARS) to diagnose their pervasive developmental disorder and detect its severity. Children Sleep Habits Questionnaire was used to assess sleep subjectively.

Subjects and methods

Study sample:

This study was conducted on 15 Egyptian children, randomly chosen from those attending the child psychiatry out patient clinic, at the Institute of Psychiatry, Ain Shams University between the months of January and August, 2004. Children were diagnosed through clinical history taking according to DSM-IV criteria to have a pervasive developmental disorder. Children below the age of 2 and above the age of 12 were excluded. All children meeting the diagnostic criteria whose parents agreed to participate in the study were included.

A control group, formed of 10 healthy age and sex matched children from the information bank of the sleep laboratory were obtained. The control group was matched to the patients' sex and age.

Evaluation:

A detailed clinical history was obtained from each child including family history, history of perinatal complications, presence of a developmental delay and epilepsy. The age of onset of the pervasive developmental disorders, the clinical features and any associated behavioral disturbances were noted. History of an associated medical or neurological condition in the patient or his family was also included.

The severity of the PDD was further evaluated by the Childhood Autism Rating Scale (Schopler et al., 1993). Evaluation included both an interview with the parent (usually the mother and occasionally both parents) and observation of the child. CARS is a popular tool for screening autistic children. It was shown to correctly identify up to 98% of autistic subjects and 69% of the possibly autistic as autistic (Schopler et al., 1993). It is brief, convenient and suitable for use for any child above the age of two. As most of our patients were nonverbal, and even in those with some language, verbal communication was not possible due to lack of cooperation, non verbal IQ measurements were obtained by trained psychologists.

Subjective sleep assessment was obtained through the Arabic version of Children's Sleep Habits Questionnaire (CSHQ) (Asaad and Kahla, 2001). This is 33 items questionnaire that scores sleep habits of school children as reported by the parents during the past week on a 3 point response scale (often, sometimes, rarely).

The CSHQ yields both a total score and eight subscale scores, reflecting the key sleep domains that encompass the major medical and behavioral sleep disorders in this age group.

Sleep was also objectively assessed by a polysomnogram performed at the sleep lab of the institute of psychiatry, Ainshams University. The child's mother attended the study to comfort the child and put him/her to sleep. The study was also attended by a technician who assured that the electrodes were properly attached all through the study and readjusted them when needed. All medications, except antiepileptics in some patients were stopped before the study.

Statistics:

The data was collected and analyzed with the aid of the program Statistical Package for Social Sciences (SPSS). Quantitative data were described using range, mean and standard deviation. Comparison between the groups was done using Chi square test with Yate's correction.

Results:

The sample included 5 females and 10 males. Their age ranged from 2 to 11 years with a mean age of 5.3 and a standard deviation (SD) of 2.16. Thirteen were diagnosed as autistic disorder, one as Rett syndrome and one as childhood disintegrative disorder.

Family and Past History:

None of the children in this study showed a family history of autism. Perinatal complications were reported in 7 patients (46.7%) and these included Caesarian section (2 patients), breech presentation (1 patient), history of neonatal ICU admission (2 patients), delayed cry (2 patients), low birth weight (2 patients), neonatal cyanosis (2 patients), and maternal gestational diabetes mellitus in one patient.

The developmental history of these children showed normal developmental milestones till the onset of the behavioral disturbance in six of the patients (40%). In the rest (60%), developmental delay in at least one area of development (motor, mental, social or language milestones) was reported.

The medical history of the children revealed one case of Fragile X syndrome, one case of infantile spasms (West syndrome), and one child with history of ambiguous genitalia and dysmorphic features in the form of hypertolerism and low set ears. The chromosomal count of this child was normal.

Epilepsy and Autism:

Epilepsy was reported in 7 (46.7%) patients in this study. Types of seizures included generalized tonic clonic seizures in one patient, adversive fits in two patients, infantile spasms in one patient, generalized tonic seizures in one patient and absence in one patient. Of these, only 5 had an available EEG. The abnormalities detected included bilateral temporal foci in one patient, frontal focus in one patient, generalized epileptic activity in one patient and no abnormality in two patients. Epilepsy was controlled in all patients with no fits occurring in the last month prior to the study.

Behavioral Disturbances:

In 7 patients (46.7%) the parents reported that the behavioral abnormality dated since birth. Onset was before the age of two in 66% and was before the age of three for all the patients in our study. Hyperactivity was reported in 8 patients (53.3%), aggression in 3 patients (20%), and self injurious behavior in 6 patients (40%) in the form of head banging or hand biting, but more severe forms of self injury were not found. The main clinical features of the cases are outlined in Table 1.

IQ:

The IQ of patients in this study ranged from 24 to 75 with a mean of 46.2 and SD of 14.7. Only one patient had an IQ above 70 while all other patients were mentally subnormal. There was no significant correlation between perinatal complications and severity of intellectual disability or incidence of epilepsy. At the same time there was no significant correlation between incidence of epilepsy and perinatal complications.

Results of CARS:

Childhood Autism Rating Scale (CARS) was used to assess the severity of pervasive developmental disorder in the children. The severity of the condition showed no significant correlation to gender. Ratings for the various CARS subscales (table 2).

Results of CSHQ:

The children's sleep habits questionnaire (CSHQ) showed that sleep duration was adequate in 93.3% of patients. Sleep related anxiety was seen in 53.3% of patients and night awakening in 40% of patients. Nocturnal enuresis was seen in 20% of patients (3 patients) and increased movements during sleep in 26.7% (4 patients). Sleep bruxism was seen in 20% of patients (3 patients), while sleep disordered breathing occurred in one patient (table 3).

Parents reported that no or mild bed time resistance was seen in 60% of patients while bed time resistance was moderate in 26.7% of cases and severe in 13.3% of cases. Sleep latency was mildly affected in 73% of cases and moderately prolonged in 6.,7% of cases. Severely increased sleep latency was seen in 20% of patients. Moderate day time sleepiness was seen in 6.7% of patients while mild or no daytime sleepiness was seen in the rest of patients (tables 4).

There were no significant correlations between sleep anxiety or night awakening and severity of PDD.

Results of Polysomnography:

As compared to age and sex matched control, the polysomnogram has shown a significant decrease in sleep efficiency, prolongation of stage 1 and 2 NREM sleep and shortened REM sleep in patients with PDD. The arousal index and number of awakenings were significantly higher in children with PDD than in the control group. The PLMS index was also significantly higher in the patient than the control group. Three of the patients with a periodic leg movement during sleep index (PLMS I) above one were reported by the parents to be hyperactive during the day while three of the patients with a PLMS index above one were reported by the parents to have increased movement during sleep (table 5, figures 1 and 2).

The results of our study showed a highly significant decrease in sleep efficiency and increase in arousal index in patients with moderate PDD than those with mild PDD. This is shown in *table 6*. However, no correlation was found between IQ and either of these sleep parameters. Also there was no correlation between number of awakening, stage 1, stage 2 or REM percentage with either the IQ and the severity of PDD.

Table 1: The main clinical features of the patients

	Present		Absent	
	No	%	No	%
Epilepsy	7	46.7	8	53.3
Hyperactivity	8	53.3	7	46.7
Perinatal complications	7	46.7	8	53.3
Normal early development	6	40	9	60
Aggression	3	20	12	80
Self injury	6	40	9	60

Table 2: Occurrence of various symptoms in the patients as detected by CARS

	Absent%	Mild %	Moderate%	Severe%
Relating to people	13	46	33.3	6.7
Imitation	20	40	26.7	13.3
Emotional response	20	46.7	33.3	0
Body use	33.3	13.3	46.7	6.7
Object use	0	60	33.3	6.7
Adaptation to change	53.3	40	6.7	0
Visual response	20	46.7	33.3	0
Listening response	20	66.7	13.3	0
Touch, smell and taste	46.7	46.7	6.7	0
Fear or nervousness	26.7	40	26.7	6.7
Verbal communication	0	13.3	33.3	53.3
Nonverbal Communication	6.7	26.7	60	6.7
Level of activity	6.7	33.3	53.3	6.7
Intellectual response	6.7	26.7	53.3	6.7
General impression	0	53.3	40	6.7
Total score	0	60	40	0

This table shows the percentage of patients showing mild, moderate and severe symptoms in each of the items of the childhood autism rating scale (CARS).

Table 3: The occurrence of sleep disturbances in patients as detected by CSHQ

	Present		Absent	
	No	%	No	%
Adequate sleep duration	14	93.3	1	6.7
Sleep anxiety	8	53.3	7	46.7
Night awakening	6	40	9	60
Breathing disorders	1	6.7	14	93.3
Nocturnal enuresis	3	20	9	80
Increased movements	4	26.7	11	66.3
Sleep bruxism	3	20	12	80

Table 4: The severities of some sleep parameters in the patients as detected by CSHQ

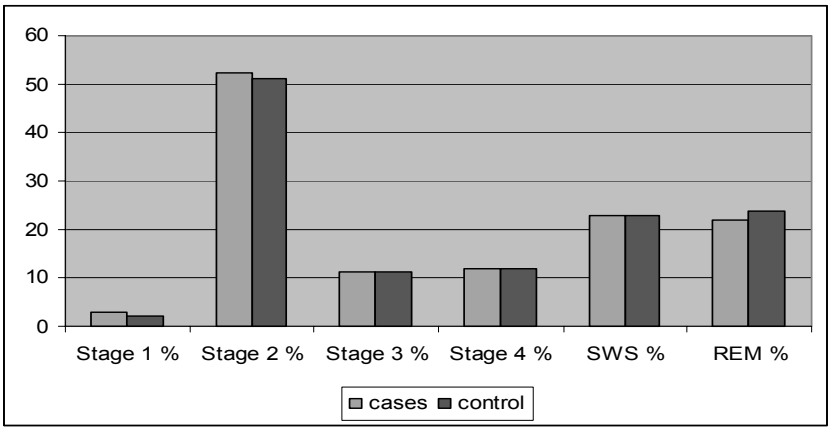
	Mild %	Moderate %	Severe %
Bed time resistance	60	26.7	13.3
Sleep latency	73.3	6.7	20
Day time sleepiness	93.3	6.7	0

Table 5: Polysomnography findings in patient and control groups

Sleep parameter	Cases		Control		t	P	Significance
	Mean	SD	Mean	SD			
Sleep efficiency. %	85.83	4.93	92.66	2.17	4.09	<0.01	HS
Stage 1 %	2.91	0.58	2.03	0.23	4.50	<0.01	HS
Stage 2 %	52.24	1.07	51.20	0.83	2.59	<0.05	S
Stage 3 %	11.36	0.86	11.31	0.34	0.17	> 0.05	NS
Stage 4 %	11.80	0.73	11.96	0.40	0.62	> 0.05	NS
SWS %	22.96	1.23	22.88	0.51	0.19	> 0.05	NS
REM %	21.94	1.15	23.89	1.22	4.01	<0.01	HS
SWSL	27.86	2.97	29.20	1.22	1033	> 0.05	NS
REML	66.46	5.13	67.10	4.01	0.32	> 0.05	NS
REM D	17.48	0.79	17.90	0.44	1.48	> 0.05	NS
Arousal I	0.86	0.39	0.47	0.25	2.73	<0.01	HS
Number of awakenings	1.60	1.12	0.10	.316	4.09	< 0.01	HS
Apnea index	8.66	0.22	0.00	0.00	1.21	> 0.05	NS
Obstructive apnea	6.66	0.17	0.00	0.00	1.16	> 0.05	NS
Mixed apnea	1.33	5.16	0.00	0.00	0.81	> 0.05	NS
Apnea hypoxia index	5.33	0.20	0.00	0.00	0.81	> 0.05	NS
PLMS I	0.92	0.48	0.41	0.24	3.05	<0.05	S

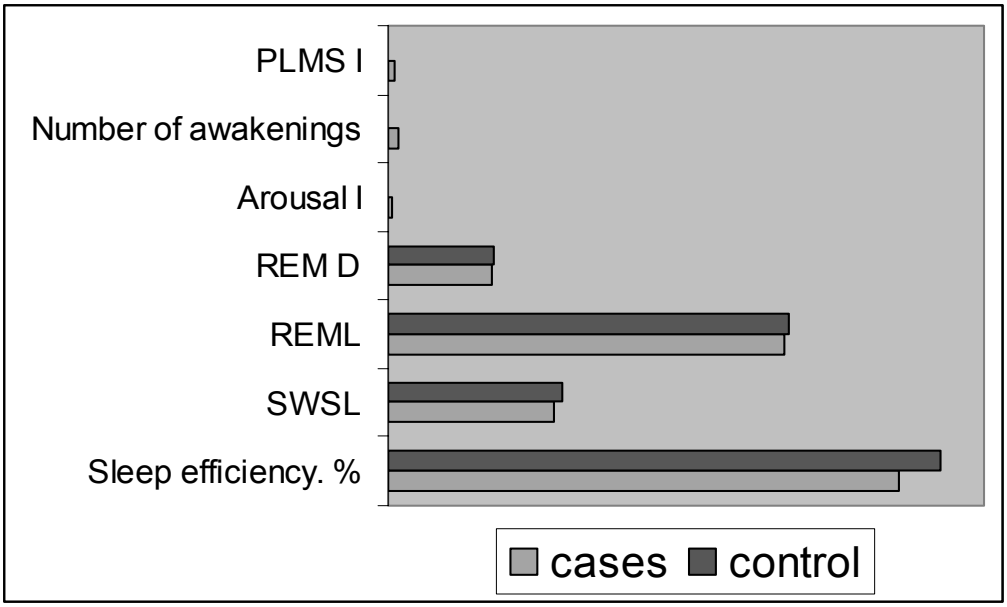
This table compares the various sleep parameters detected by polysomnography in the patient and control groups. REM= rapid eye movement; SWS= slow wave sleep; REML= rapid eye movement latency. SWSL= slow wave sleep latency; REMD= rapid eye movement density ;arousal I = arousal Index. PLMS I= periodic leg movement during sleep index. P>0.05= non significant; P<0.05= significant; P<0.01= highly significant

Figure 1: Comparison between various sleep stages in patients and controls



This figure shows the difference between percentages of different sleep stages in cases and controls. Stages 1 and 2 of NREM sleep are significantly longer while REM sleep is significantly shorter in cases than in control; SWS=slow wave sleep; REM= Rapid eye movements

Figure 2 : Comparison between various polysomnographic parameters in patients and control



This figure shows the difference between different polysomnographic parameters in case and control groups. A significant difference is seen in PLMS index, number of awakening, arousal index and sleep efficiency; PLMS=periodic leg movements during sleep; REM D= Rapid eye movements density, REML= rapid eye movements latency; SWSL= slow wave sleep latency.

Table 6: Polysomnographic findings in patients with mild and moderate autism

	Mild		Moderate		T	P	Significance
	Mean	SD	Mean	SD			
Sleep Efficiency %	87.22	3.78	87.22	5.4	2.00	<0.05	S
Stage 1 %	2.72	0.45	2.72	0.67	1.63	> 0.05	NS
Stage 2 %	52.21	0.56	52.21	1.64	0.15	> 0.05	NS
REM %	22.10	1.21	22.10	1.12	0.61	> 0.05	NS
PLMS Index	0.9	0.54	0.9	0.43	0.18	> 0.05	NS
Arousal index	0.7	0.26	0.7	0.45	2.15	<0.05	S
Number of awakenings	1.33	1.11	1.33	1.09	1.14	> 0.05	NS

This table c*ompares the various sleep parameters detected by polysomnography in patients with mild and moderate autism. A significant difference is seen in sleep efficiency and arousal index. REM= rapid eye movement; PLMS I= periodic leg movement during sleep index. P>0.05= non significant; P<0.05= significant*

Discussion

The pervasive developmental disorders (PDD) are characterized by delay and deviance in the development of social skills, language and communication, and a restricted behavioral repertoire (Sadock and Sadock, 2004). Children with PDD show a number of associated behavioral disturbances including sleep disturbances that are quantitavely and qualitatively different from those exhibited by normal children and those with other psychiatric disorders (Patzold et al., 1998).

Despite the high prevalence of sleep disturbances in children with PDD, only a few polysomnographic studies in autistic children are available in the literature (Tanguay, 1976; Thermulai et al., 2002; Sun et al., 2003) and the number of subjects in each of these studies is small (8 to 17 patients). An even smaller number of studies included polysomnography in Asperger syndrome (Godbout et al., 2000; Tani et al., 2004) and no studies included children with childhood disintegrative disorder or PDD-NOS. Rett syndrome was more extensively studied (Segawa and Nomura, 1990, Espinar-Sierra et al., 1990, Fujino and Hashimoto 1990; Segawa and Nomura, 1992; Marcus et al., 1994; Kohyama et al., 2001).

Our study aimed at describing sleep patterns in a sample of Egyptian children with pervasive developmental disorders. Children were assessed by means of a clinical history and CARS to diagnose their PDD and detect its severity. Children Sleep Habits Questionnaire was used to assess sleep subjectively. The parents are instructed to answer the questionnaire based on the child's sleep habits in the last week. This allows evaluation of the child's sleep habits at home over a relatively long period of time which could not be assessed by the polysomnogram alone. It is also useful for

evaluating events that do not occur every day as nocturnal enuresis and other parasomnias. This was followed by objective sleep assessment by polysomnography. This allowed studying sleep architecture and verifying the data obtained by the questionnaire.

Fifteen children (10 males and 5 females) were chosen randomly from the Child psychiatry out patient clinic of the institute of psychiatry, Ain Shams University Hospital. The male to female ratio in our sample is consistent with various epidemiological studies showing a higher prevalence of autism in males (Fombonne, 1998). The relatively young mean age of the patients (5.3 SD2.16) is well suited to the aim of this study as sleep problems are reported to be more common in younger children (Patzold et al., 1998). Of the children in this study 13 were diagnosed as autistic disorder, one met the criteria for childhood disintegrative disorder and one was diagnosed as Rett syndrome.

Two of the children in our study had a known associated medical condition. One of the children had Fragile X syndrome and the other West syndrome. Another child had dysmorphic features and ambiguous genitalia which are highly suggestive of a chromosomal abnormality. Chromosomal count was normal in this child but a more detailed study for structural chromosomal abnormalities was not available and these can not be excluded. These findings reflect the heterogeneous nature of autism and are to be expected in any clinical sample. Both fragile X and West syndrome were previously associated with sleep abnormalities. For both our patients, different sleep parameters were within one standard deviation from that obtained for the PDD group as a whole, and no specific features could be detected.

Mental sub-normality is a common associated feature in PDD that has been previously associated with disturbances in sleep. Polysomnographic studies showed a reduction of REM sleep percentage, a prolonged latency of the first REM period, a reduction of the number of REM cycles and the presence of undifferentiated sleep in mentally subnormal children. The lack of high functioning autism in our sample, with only one child with an IQ above 70, and the small sample size made it impossible to isolate the effect of mental retardation on the results of our study.

Epilepsy, a common co-morbid condition in patients with PDD, may also affect sleep pattern. In this study, 43.3% of children were reported to have epilepsy. Although chronic epilepsy was previously reported to cause disturbances in sleep architecture (Shouse, 1994), most of the effect was attributed to seizures occurring on the night of the study. There is no generalized agreement considering the influence of seizures taking place prior to the night of the study on the sleep pattern (Lopez Gomez et al., 2004). Most of our patients are well controlled and none of them had any seizure in the month before the study, thus the effect of epilepsy on sleep architecture is expected to be minimal. Five of our patients were on antiepileptic medication on the time of the study including valproate and carbamazepine, and ACTH injections. Carbamazepine was previously shown to decrease REM sleep as well as the frequency and duration of periods of wakefulness while sodium valproate increases deep sleep in children (Nicholoson, 1994). Most available studies on the effects of antiepileptic medications on sleep were carried on epileptic patients

and it is not clear whither the effects of these drugs are due to a primary effect on sleep architecture or to suppression of epileptic activity. All other drugs taken by the patients were stopped at the night of performing polysomnogram. However, the chronic effects of medication or effects of withdrawal of medications on sleep can not be eliminated.

Children in our study were classified as mildly autistic or moderately autistic by the CARS. The lack of severely affected patients is probably due to the small sample size. The most commonly encountered symptom was disturbance in verbal communication (severely affected in 53.3% and moderately affected in 33.3%). This could be explained by the fact that delayed language development is the most common presenting feature of autism (Campbell and Shay, 1995) and the most alarming to the parents.

In previous studies parents reported a variety of sleep disturbances in autistic children, with disorders in initiation and maintenance of sleep being the most common. These manifested as extreme sleep latencies, shortened sleep times and frequent awakening (Thermulai et al., 2002). However, most of the patients (60%) in our study were reported to have within normal sleep latencies by their parents and 26.7% reported a moderate increase in sleep latency. The parents also reported that 93.3% had adequate sleep hours although 40% of the children woke up at least once during the night. It is not clear whither the differences between the results of our study and previous reports reflect a true difference in the pattern of symptoms, a cultural difference in sleep habits or a difference in parental report and reaction to their children's behavior.

Sleep related anxiety was reported in 53% of patients in our study and this showed no correlation with severity of autism. Anxiety is a prominent feature in many children with autism and may contribute to sleep problems (Richdale, 1999). The role of anxiety was believed be more in older children and those with a higher IQ (Richdale and Prior, 1995) and in patients with Asperger syndrome (Tani et al., 2004). The result of our study indicates a high level of anxiety even in younger children with low IQ.

Seven (43.3%) of the children in our study were reported to have a paroxysmal event during sleep by the parents. This is consistent with a large study conducted by Yu and Miles on 163 patients with autism in which parasomnias occurred in 77.3% of patients (Yu and Miles, 2002). In our study three cases of sleep bruxism (20%), three cases of nocturnal enuresis (20%), and four cases (26.7%) of increased movements during sleep were reported by the parents. The polysomnogram showed a significant increase in PLMS index in patients with PDD compared to control.

Bruxism, or the intermittent grinding or clenching of teeth during sleep is a common phenomenon. Yu and Miles found bruxism in 24.5% of patients with autism (Yu and Miles, 2002) which is consistent with the results of our study. The exact etiology of bruxism is not known, however, pharmacologic evidence suggests that the central dopaminergic system may be involved in the pathophysiology of sleep bruxism. Recent studies indicate that bruxism may represent a mild manifestation of REM sleep behavior disorder (RBD). This is particularly interesting in the light of the recent detection of RBD, another dopamine dependent disorder, in five

children with autism and insomnia (Thermulai, 2002).

Periodic limb movements are defined as involuntary repetitive movements that occur primarily during stage 1 and 2 sleep. Our study has shown a significantly higher PLMS index in children with PDD than the control group. However, it was not elevated enough to diagnose PLMS in any of these children. Previous studies have also shown an increased incidence of PLMS in children with autism (Thermulai, 2002, Schreck, 2004). PLMS was previously associated with ADHD and Sun et al reported PLMS in a child with autism and comorbid ADHD (Koherman and Carney, 2000; Sun et al., 2003). Of the seven children with an elevated PLMS index in our study, three were reported by the parents to have increased movements during sleep, but no statistically significant association was found between increased daytime activity and PLMS index.

Although these problems appear as separate items, sleep bruxism, PLMS and RBD are all related to disturbed motor control during sleep. This raises the probability of a specific type of sleep related impairments in CNS motor areas for children with autism and mental retardation (Schreck and Mulick, 2000). Other features that may reflect abnormal motor control during sleep were previously reported in children with autism, including increased dispersed rapid eye movements occurring out of bursts of rapid eye movements, an increased amount of muscle twitches as well as presence of rapid eye movements during stages 1 and 2 of NREM sleep (Diomedi et al., 1999).

Bruxism may be related to hyper function of dopamine, while PLMS may be related to hypofunction of dopaminergic neurotransmission (Montplaisir et al., 1994). Abnormalities in dopamine turnover have been detected in patients with PDD (Takahashi et al., 2001). A hyperdopaminergic function of the CNS might explain the hyperactivity and stereotyped behavior in autism and the response to dopamine receptor antagonists as haloperidol (Kaplan and Sadock, 1998). On the other hand, PET studies have demonstrated low medial prefrontal dopaminergic activity in some patients with autism (Herring et al., 1999).

Nocturnal enuresis was found in three (20%) of the children in our study. High frequencies of nocturnal enuresis were previously reported in children with PDD (Yu and Miles, 2002; Sun et al., 2003). The higher frequency of nocturnal enuresis in children with PDD can thus be explained as part of the general delay of development in these children. The findings in our study are consistent with this explanation as the three enuretic children showed delayed developmental milestones.

Our study has shown a highly significant decrease in sleep efficiency and increase in night awakening in patients with PDD than in the control group. This is in agreement with most of the previous studies on autism (Wiggs and Stores, 2004). Our study also showed a highly significant decrease in sleep efficiency and increase in arousal index in patients with moderate autism than those with mild autism, but no correlation with IQ. The correlation between these parameters and the severity of autism may reflect either a true worsening of the sleep efficiency with more severe autism, or an increased sensitivity of more severely autistic children to the changes in environment.

Sleep architecture showed prolonged stage 1 and 2 NREM sleep percentages and

decreased REM sleep percentage as compared to control. Changes in sleep architecture were previously reported in children with autism, but there are some controversies in the results of different studies.[15,16] Sun et al found a decreased REM percentage which is in agreement with the results of our study.[18] Unlike findings of Elia et al and Diomedi et al, there was no difference in REM density between the patient and control group in our study and no correlation between REM % and IQ. The prolongation in stages 1 and 2 seen in our study has not been previously reported (Diomedi et al., 1999; Elia et al., 2000).

The establishment of a mature sleep wake rhythm is a developmental phenomenon and this could account for the greater prevalence of sleep disorders in children with developmental disabilities in general. Significant sleep fragmentations, manifested by frequent awakenings and arousals were detected in children with PDD in our study. Although hyperactivity is a common symptom in autism, occurring in 53.3% of patients in our study, sleep patterns similar to those previously reported in ADHD were not found. This probably reflects the difference in the pathological and biochemical nature of the two disorders.

The results of our study thus confirm the presence of sleep disturbances in children with PDD. The study of sleep in children with pervasive developmental disorders may be rewarding in more than one way. First, it helps the families deal with a disturbing symptom. Second, sleep disturbances may affect daytime achievement. A recent study by Schreck and co-workers (2004) has shown that sleep problems predicted more intense symptoms of autism. In addition sleep problems have been consistently shown to negatively influence learning rate and cognitive performance in typically developing children and adults. Eliminating sleep problems, whatever their cause may aid these children achieve their full potential.

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Acute Phase Reactants (Proteins) in Schizophrenia

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Abstract

A great number of studies show biological alterations in patients with schizophrenia, but many of these data are conflicting. Schizophrenia is a vastly heterogeneous disorder, most likely not caused by one etiological factor, but rather due to a complex network of different, interacting pathogenic influences. There are changes occurring in the immune system as well as the acute phase reactants. This study was carried out on 25 patients diagnosed as non paranoid schizophrenia and 10 controls. The results showed that there is no difference in the scores of the patients and controls. These results show that the process of schizophrenia is more on an immunological level than on an inflammatory level. Further in depth studies on these changes in recommended.

Introduction

Acute-phase reactants (proteins) are a class of plasma proteins whose plasma concentrations increase (positive acute phase proteins) or decrease (negative acute phase proteins) in response to inflammation. This response is called the acute-phase reaction. The levels of these proteins alter in response to tissue injury, inflammation, malignancy and psychological conditions.

Local inflammatory cells (neutrophil granulocytes and macrophages) secrete a number of cytokines into the bloodstream, most notable of which are the interleukins IL-1, IL-6 and IL-8, and TNF-alpha.

The liver responds by producing a large number of acute-phase reactants, most notable of which are: C-reactive protein (CRP), mannose-binding protein, alpha 1-antitrypsin, alpha 1-antichymotrypsin, alpha 2-macroglobulin, some coagulation factors (Fibrinogen, prothrombin, factor VIII, von Willebrand factor, plasminogen), complement factors, ferritin, serum amyloid P component, serum albumin concentrations fall in acute disease states. For this reason albumin is sometimes referred to as a negative acute phase protein (Pepys and Hirschfield, 2003).

Measurement of acute phase proteins is a useful marker of inflammation.

1) CRP is a member of the class of acute phase reactants as its levels rise dramatically during inflammatory processes occurring in the body. It is thought to assist in complement binding to foreign and damaged cells and affect the humoral response to disease. It is also believed to play an important role in innate immunity, as an early defense system against infections. C-reactive protein is a test of value. Marked rises in CRP reflect the presence and intensity of inflammation.

ESR provides a non-specific screening test for the presence of an acute phase reaction.

Although the ESR and CRP may be valuable indicators of an acute phase response, normal results do not exclude active disease.

2 Mannose-binding proteins is a soluble factor in the human body that binds mannose residues to pathogens. It is part of the immune system's defenses against

bacteria. It is produced in the liver as a response to infection, and is part of many other factors termed acute phase proteins. Mannose-binding protein may also be referred to as mannan binding lectin.

3 Alpha 1-antitrypsin or α_1-antitrypsin (A1AT) is a serine protease inhibitor (serpin). It protects tissue from enzymes from inflammatory cells, especially elastase, and is present in human blood at 1.5 - 3.5 gram/liter. A1AT is a 52 kDa serine protease inhibitor, and in medicine it is considered the most prominent one, given the fact that the words α1 antitrypsin and protease inhibitor (P_i) are often used interchangeably.

4 Alpha 1-antichymotrypsin is a alpha globulin glycoprotein and serpin

5 Alpha-2 macroglobulin is a large plasma protein found in the blood. It is produced by the liver, and is a major component of the alpha-2 band in protein electrophoresis.

6 Fibrin is a protein involved in the clotting of blood. Fibrin is made from its zymogen fibrinogen, a soluble plasma glycoprotein that is synthesized by the liver.

7 The complement system is a biochemical cascade of the immune system that helps clear pathogens from an organism. It is derived from many small plasma proteins that work together to form the primary end result of cytolysis by disrupting the target cell's plasma membrane.The actions of the complement system affects both innate immunity and acquired immunity. Activation of this system leads to cytolysis, chemotaxis, oposonization, immune clearance, and inflammation, as well as the marking of pathogens for phagocytosis.

8 Serum Amyloid P component (SAP) is the identical serum form of Amyloid P component (AP). AP is thought to be an important contributor to the pathogenesis of a related group of diseases called the amyloidoses. (Retrieved from http://en.wikipedia.org/wiki).

A great number of studies show biological alterations in patients with schizophrenia, but many of these data are conflicting. Schizophrenia is a vastly heterogeneous disorder, most likely not caused by one etiological factor, but rather due to a complex network of different, interacting pathogenic influences. Variable clinical pictures may reflect different etiological factors. In a comprehensive theory of the origin of schizophrenic disorders, genetic and environmental influences cause changes in neuronal development which result in functional alterations of different neurotransmitter systems. Immunological research in schizophrenia was initially based on the "infection hypothesis" which was triggered by observing schizophrenia-like psychoses after influenza pandemic. Numerous immunological studies focusing on antibodies against specific viruses, unspecific antibodies and different other immune-phenomena were carried out in schizophrenia patients. Although the variability of the results from these studies is strikingly high, subgroups of patients with schizophrenia show an activated inflammatory response system with increased levels of proinflammatory cytokines and acute phase proteins. Furthermore, some investigations find changing activities in the T-cell system with a shift of TH-1 to an increased TH-2 activity. Endocrinological factors which may play a relevant role in the etiopathogenesis of schizophrenia include sex hormones and all changes caused by stress or other influences which are directly related to the HPA-axis. Alterations of the

immune and the endocrinological systems might be caused by environmental factors like infections or exogenous stress. Due to the intensive interaction between the central nervous system, the immune system and different hormones the "development of a pathology" like schizophrenia can be seen in an integrative but multifactorial fashion. The clinical manifestation, the severity and the course of the disease might then be modulated by genetic vulnerability, the time of the "primary insult" -- which could be an infection or psychological stress -- and its neuronal localization and intensity. Different compensatory and decompensatory mechanisms in later life very likely play a crucial role for the further course of the disorder (Sperner, 2005)

In this study we tried to evaluate the levels acute phase proteins in a sample of Egyptian patients suffering from schizophrenia.

Subjects and Method

This study was carried out at the Institute of Psychiatry, Ain Shams University Hospitals over a period of 5 months. The study included 25 patients (18 males and 7 females), as well as 10 controls (4 females and 6 males). The inclusion criteria for the patients were:

Inpatients at the Institute of Psychiatry Ain Shams University Hospitals.

Ages between 21 and 41 years

Both males and females patients were included

Patients were diagnosed as suffering from non-paranoid schizophrenia according to the ICD-10 Research and Diagnostic Criteria (1993) using the ICD-10 symptom checklist (1994). Non-paranoid schizophrenia was chosen as most of the studies show that these forms of schizophrenia are richer in structural brain changes as well as brain imaging changes and genetic findings which will lead them to have more immunological and inflammatory changes, while the paranoid form is more environmentally determined.

All laboratory tests were done within 48 hours of admission after being diagnosed and before starting treatment.

All patients were not taking any medication for at least 6 weeks and did not receive any ECT sessions at least 6 months prior to joining the study.

Informed consent was taken from patients or their families to join the study.

The entire patient group had no co-morbid medical illness, or co-morbid axis 1 psychiatric diagnosis, or substance use disorder.

A control group selected from the employees of the institute of psychiatry were matched to age, sex and educational level of the patient group and had no medical illness, or psychiatric morbidity assessed by the general health questionnaire (GHQ) (Goldberg, 1988) in its Arabic version (Okasha, 1988). The entire control group gave their consent to participate in study.

ESR, C reactive protein, Alpha 1 antitrypsin, Fibrinogen and Complemet 3 were evaluated for all patients and controls, however, Haptoglobin, Alpha 1 antichymotrypsin and Ceruloplasmin from the acute phase reactants were not assessed due to unavailability of the kits at the time of the study.

All laboratory investigations were carried out at the Institute of Psychiatry laboratory,

where ESR was measured in mm/hr at 20 degrees + or – 3 degrees.

C_3 and AAT were estimated by Radial immuno diffusion (RID) plates (manufactured by Biocientifica S.A.) Serum samples were collected and stored at – 20^{o}C using Berne Method (1974).

C- reactive protein was detected by Latex Seralogy Test (Avitex) from omega diagnostics LTD when latex suspension coated with antibodies to human CRP is mixed with serum, clear agglutination is seen within 2 minutes (Ward, 1975).

Erythrocyte sedimentation rate was done using the Westergren method.

Fibrinogen was assayed by Multifibrin U test (Dadebehring) using fibrintimer.

Results

In this study the mean age for the patient group was 27.56 (±4.37), while that for the control group was 27.30 (±4.40). Out of the 25 patients 18 were males (72%) and 7 were females (28%), while in the control group, out of the 10 controls 6 males (60%) and 4 females (40%) (Figures (1) and (2) respectively).

Regarding the ESR levels the mean level in the patient group was 14.84 (±11.14), while that of the control group was 13.30 (±11.68) with no significant difference.

Comparing the results of both groups as regard the acute phase reactants, we found that the C reactive protein was negative in 24 patients out of the 25 and was also negative in the control with no significant difference.

The fibrinogen mean level result was 2.88 g/l (±1.60) in the patient group and 2.64 g/l (±0.89) in the control group with no significant differences between both groups.

There was also no significant difference between both groups regarding the mean level of C3, which was 144.80 mg/dl (±30.33) in the patient group and 145.10 mg/dl (±52.12) in the control group.

Similarly, no significant differences were found between both groups regarding the mean level of Alpha 1-antitrypsin (A1AT), which was 173.96 mg/dl (±33.43) in the patient group and 173.10 mg/dl (±44.25) in the control group (Table (1) and Figure (3)).

Figure (1)

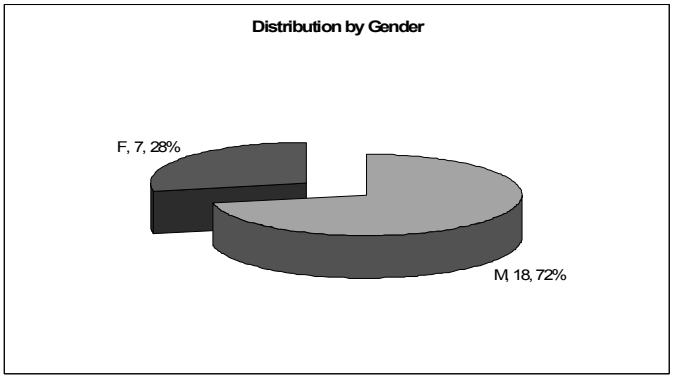


Figure (2)

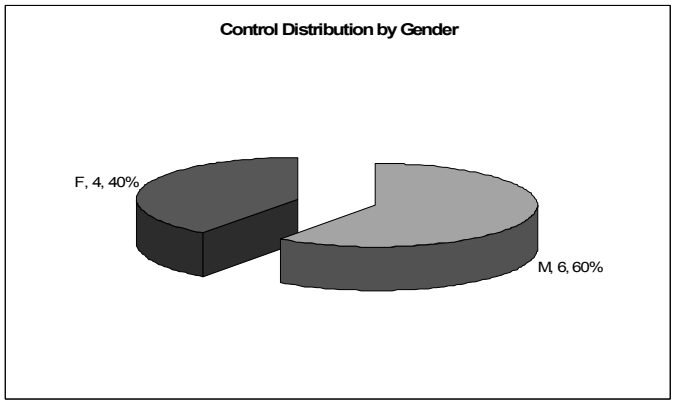
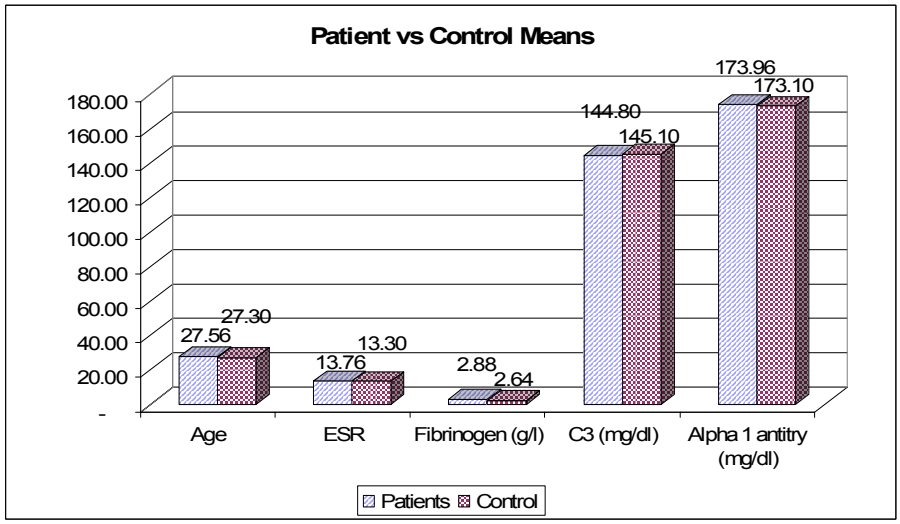


Table (1) shows the comparison of the different mean levels of acute phase reactants (ESR, fibrinogen, C3 and A1AT) between both the patient and the control groups.

Item	Patient group	Control group
ESR	14.84 (±11.14)	13.30 (±11.68)
Fibrinogen (g/l)	2.88 (±1.60)	2.64 (±0.89)
C3 (mg/dl)	144.80 (±30.33)	145.10 (±52.12)
A1AT (mg/dl)	173.96 (±33.43)	173.10 (±44.25)

Figure (3) shows the differences in mean levels of age, ESR, fibrinogen, C3 and A1AT in both the patient group and the control group with no significant difference between both groups.

Figure (3)



Discussion

A working model to understand schizophrenia would help understanding the process of the disorder. It is suggested that DNA, gene expression, viruses, toxins, nutrition, birth injury and psychological experiences all play are role in the aetiology of schizophrenia. These aetioligical factors lead to the pathophysiology of the disorder mainly affecting the brain development which includes neuron formation, migration, pruning, and apoptosis. This will in turn lead to affection of the neural connectivity and communication causing impairment in the fundamental cognitive process (thinking) causing impairment in the second order cognitive processes which include attention, memory and language. All this will lead to the appearance of the symptoms of schizophrenia. This working model helps us take into account all the different factors that may be involved in the schizophrenia process (Okasha, 2006).

There is a growing body of opinions affirming schizophrenia is a spectrum disease covering several conditions of different aetiology. Various studies have recently shown immunological changes in schizophrenia, and an immune pathogenetic hypothesis has gained acceptance. In a study carried out by Mazzarello etal. (2004), they analyzed with a relatively wide approach the immunological dysfunction in schizophrenia, focusing in particular on lymphocytes morphology and subset distribution. They performed in peripheral blood samples of 24 schizophrenic patients, assessment of acute phase proteins and immunological variables and found an increased serum CRP concentration (mg/ml), which is different from the results of our study since the timing of sampling was different in both studies. Also, the difference in patient sample where they included all subtypes of schizophrenia, while in our study non-paranoid schizophrenia was chosen as most of the studies show that these forms of schizophrenia are richer in structural brain changes as well as brain imaging changes and genetic findings which will lead them to have more immunological and inflammatory changes, while in comparison the paranoid form of schizophrenia is more environmentally determined.

An acute phase protein (AP) response has been reported in major depression. In order to examine whether an AP response occurs in other psychiatric disorders, such as schizophrenia and mania, Maes etal. (1997) measured plasma acute phase proteins such as haptoglobin (Hp), immunoglobulin G (IgG), IgM, fibrinogen (Fb), complement component 3 (C3C), C4, alpha 1-antitrypsin (alpha 1 AT), alpha 1-acid-glycoprotein (alpha 1S) and hemopexin (Hpx), in 27 schizophrenic, 23 manic, 29 major depressed and 21 normal subjects. Schizophrenic patients had significantly higher plasma Hp, Fb, C3C, C4, alpha 1S and Hpx than normal controls. Manic subjects showed significantly higher plasma Hp, Fb, alpha 1S and Hpx than normal volunteers. Depressed subjects had significantly higher plasma Hp, Fb, C3C, C4 and alpha 1S than normal controls. Overall, the above disorders in AP reactants were more pronounced in schizophrenic than in depressed subjects. No significant differences in the above AP reactants could be found between normal volunteers, and schizophrenic, manic or depressed patients who underwent chronic treatment with psychotropic drugs. The results suggest that not only major depression but also schizophrenia and mania are accompanied

by an AP response, and that the latter may be suppressed by (sub) chronic treatment with psychotropic drugs.

Chiu and his colleagues (1999) studied a common polymorphism in the alpha1-antichymotrypsin (ACT) gene which is associated with Alzheimer's disease. ACT is also a trophic factor in the hippocampal neurons. In order to examine if the ACT gene plays a role in the pathogenesis of schizophrenic disorders, patients (n = 175) and control subjects (n = 114) were genotyped for ACT. The results demonstrated no association between schizophrenia and cognitive deficit in schizophrenia and ACT polymorphism. The data suggest that the ACT gene is not of major importance for the genesis of schizophrenia. In our study we were not able to study the antichymotrypsin since the laboratory kits were unavailable but from the negative results we reached in the other acute phase proteins we can say that the results would have been similar for antichymotrypsin.

In a study carried out by Wong et al. (1996) measuring the changes in the concentration of some serum acute phase proteins (alpha 1-antitrypsin, alpha 2-macroglobulin, complement C3, haptoglobin, ceruloplasmin, transferrin, albumin and hemopexin, thyroxine-binding globulin, retinol-binding globulin, plasminogen and Gc-globulin) are reported in two separate series of Chinese, male schizophrenic patients and healthy controls. In the first series, 41 healthy blood donors and 98 schizophrenic patients in different stages of the disease were investigated. The second series consists of a random sample of 50 acutely ill schizophrenic patients and a second group of healthy subjects. The concentrations of these serum proteins were measured by rocket immunoelectrophoresis in agarose gel. Increased levels of serum alpha 1-antitrypsin, alpha 2-macroglobulin, haptoglobin, ceruloplasmin, and thyroxine-binding globulin were observed in both series of patients when compared to their respective controls. Albumin, transferrin and retinol-binding protein levels were reduced in patients in both series. Hemopexin levels were increased only in the acutely ill patients while complement C3 was decreased in the chronically ill patients. No changes were observed in the Gc-globulin levels of all groups of patients. With the exception of complement C3, the changes observed in the levels of these serum proteins were appropriate for that of an acute phase response. Differences from our study are due to the different laboratory methods used and the sample was carried out on Egyptian patients who have a different ethnic background and may show a different response to environmental stressors.

We can conclude from this study that the acute phase proteins are not the main changes taking place in patients with schizophrenia as there is no acute inflammatory response, but rather an earlier and more subtle immunological change which does not directly affect the acute phase proteins or elevate them to a level which can be considered as an acute inflammatory response. The differences in the results obtained from different studies suggests that there is a deficiency in the process of investigating the acute proteins, also there has been a dramatic shift to studying the different genes involved in schizophrenia and their polymorphism.

Limitations of the study

The limitation of this study rests in three main domains, first the number of patients

was limited in order to generalize these findings on all patients, secondly the patients should be in acute relapse of schizophrenia when being assessed, and thirdly a wider evaluation of the acute phase proteins and immune system changes should be carried out in future studies.

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Emotional Disturbances and Quality of Life in Type-1 Diabetic Children and Adolescents: Relation to Glycemic Control and Microvascular Complications

El Laboudy M. and Ramy H.

Abstract

Emotional disturbances, specifically depression and anxiety, constitute a major health problem in type -1 diabetic children and adolescents with marked effect on the quality of life, metabolic control and response to treatment among them. The study aims to study the frequency and severity of depressive and anxiety symptoms and their impact on quality of life in children and adolescent with type-1 diabetes mellitus (DM). The relation of these symptoms to glycemic control and diabetic microvascular complications will be also studied. The present study was conducted on 94 patients with type-1 DM (48 males and 46 females) with a mean age of 12.5 ± 3.8 years attending the Pediatric Diabetes Clinic, Children's Hospital, Ain Shams University. The patients were classified according to the degree of glycemic control (as reflected by glycated hemoglobin: HbA_1C levels) into: well-controlled group (HbA_1C: 6-7.5%), fairly-controlled group (HbA_1C: > 7.5-8.5%) and poorly-controlled group (HbA_1C: > 8.5 %). In addition to full history taking and thorough clinical examination, all patients were assessed using the Pediatric Quality of Life Inventory (Peds QL Generic Core scale) and the Pediatric Quality of Life Diabetes Module scale. Emotional disturbances were assessed using Children's Manifest Anxiety (CMA) scale and Children Depression Inventory (CDI). The poorly controlled group of diabetic patients experienced the worst quality of life and had significantly higher anxiety and depressive symptoms in comparison to the other groups with a positive correlation to disease duration, diabetic microvascular complications and frequency of hospital admission. The well-controlled group with tight glycemic control receiving intensive insulin therapy and kept on frequent home monitoring of blood glucose experienced higher worry and anxiety module scores than the fairly-controlled patients with a subsequent negative impact on the quality of life. The results of the present study indicate the importance of adequate metabolic control of DM and proper care of diabetic microvascular complications for the improvement of psychological well-being and quality of life in diabetic children and adolescents. They also point to the benefits of using an intermediate regime of glycemic control rather than the very tight regime. Regular psychiatric evaluation and psychosocial support of diabetic patients and their parents should be considered and encouraged as an integral part of diabetes care.

Introduction

Type -1 diabetes mellitus (DM) is the most frequent endocrine– metabolic disorder of children and adolescents with important consequences on physical, emotional and social development due to the disease process, treatment schedule and complications ***(Sperling 1997, Johnson and Perwein, 2001)*** The prevalence of type-1 DM among Egyptian school –age children was estimated to be between 1.09/1000 to 2/1000 ***(Ghali et al 1985, Ali et al 1986, Ghali et al 1990, and Salem et al 1990).*** The deleterious impact of type-1

DM on functional health should not be underestimated since poor functional health in children and adolescents with type -1 DM invariably leads to negative clinical and behavioral outcomes ***(American Diabetes Association, 2004)***

The prevalence of emotional disturbances (depression and anxiety) is much higher in diabetic patients than the general population with a marked impact on the control of diabetes and quality of life among these patients ***(Sadock and Sadock, 2003)*** Traditional outcome measures (morbidity and mortality) had been found to be of limited value when assessing the effect of chronic disease like diabetes on physical or psychological status of children and their families, while measures of quality of life (QoL) may provide a comprehensive account of such effect ***(Anderson et al,2003)***.

Health-related quality of life (HRQoL) refers to the physical, psychological and social domains of health that are influenced by a person's experience, beliefs, expectations and perceptions ***(Varni et al 1999, Fayers and Machi,2000).***The HRQoL in children and adolescents with type-1 DM could be influenced by many factors including the disease process, lack of glycemic control, physical complications, frequent hospital admission, complexity of treatment regimens and psychosocial compromise ***(Brown et al 2002 and Varni et al 2003).*** Emotional distress with anxiety and/or depression in type -1 DM may arise from the lack of knowledge about disease itself, the fear and worry of patients and their parents, the strict dietetic programs, the frequent home monitoring of blood glucose, and the intensive insulin therapy aiming for tight glycemic control ***(Hanna and Gutherie 2001, Hahl et al 2002, and Cameron 2003).***

Consequently, the present study was designed to evaluate the emotional status and health–related quality of life in children and adolescents with type -1 DM, and to provide psychological support for these patients and their families accordingly.

Patients and Methods

This randomized study was conducted on 94 patients with type-1 DM (48 boys and 46 girls), aged 6-18 years with mean age of 12.5 ± 3.8 years. They were attending the Pediatric Diabetes Clinic, Children's Hospital, Ain Shams University during the period between January 1st, 2004 till December 31st, 2005. The disease duration ranged from 6 months to 15 years with a mean disease duration of 8.6 ± 5.2 years. The patients were classified into two groups according to disease duration:

Group (A): included 48 patients with disease duration less than 5 years. This group composed of 28 boys and 20 girls with a mean age of 8.4 ± 2.5 years.

Group (B): included 46 patients with disease duration equal to, or more than 5 years. This group composed of 20 boys and 26 girls with a mean age of 14.2 ± 4.8 years.

The patients were further classified according to the degree of glycemic control as reflected by the mean glycosylated hemoglobin (HbA_1C) levels into:

Group I: included 24 patients with good glycemic control (mean HbA_1C was 6.0 – 7.5% during the period of the study). This group comprised 14 boys and 10 girls a mean age of 10.2 ± 4.6 years.

Group II: included 32 patients with fair glycemic control (mean HbA_1C was > 7.5 – 8.5%). This group comprised 14 boys and 18 girls with a mean age of 11.9 ± 3.5 years.

Group III: included 38 patients with poor glycemic control (mean HbA_1C was above 8.5 %). This group included 20 boys and 18 girls with a mean age of 13.2 ± 3.8 years.

Patients who had, in addition to DM, another chronic disease which may affect the quality of life as rheumatic heart disease, bronchial asthma or chronic blood disease were excluded.

All patients were subjected to:

Comprehensive history taking with particular emphasis on the age, duration of illness, dose and regimen of insulin therapy, frequency of hospital admission, number of hypoglycemic attacks or diabetic ketoacidosis (DKA) during the last year, and socioeconomic history (number of family members, job of the parents, degree of education, housing condition, income and resources).

Thorough physical and neurological examination including weight, height, body mass index (BMI), sites of insulin injection, chest, cardiac and abdominal examination. Full neurological assessment to exclude peripheral neuropathy was also included.

Laboratory investigations: to assess the degree glycemic control and diabetic complications:

Glycosylated hemoglobin (HbA_1C): Determination of the mean HbA_1C was measured as a reflection of long –term glycemic control over the preceding 10-12 weeks. High performance liquid chromatography (HPLC) using Globin Chain Analyser supplied by Bio-Rad Diagnostic Group was used for determination of HbA_1C every 12 weeks. Glycemic control in relation to HbA_1C was considered to be optimal (good) if HbA_1C is 6-7.5% suboptimal (fair) if HbA_1C is >7.5-8.5% and high risk (poor) if HbA_1C > 8.5% of adult Hb ***(ISPAD, 2000).***

Quantitative determination of urinary albumin excretion rate (Test of Microalbuminuria): Timed-overnight urine sample was collected by the patient in a plain container and taken to the hospital at the morning. Part of the fresh sample was examined to exclude urinary tract infection and overt proteinuria. Urinary albumin excretion (UAE) was assessed using the quantitative immune turbidimetric assay, and the test was repeated on three occasions one-month apart. Microalbuminuria (as an indicator of diabetic nephropathy) was defined as when two out of three samples showed an albumin excretion of 30-300ug/mg creatinine ***(ISPAD, 2000).***

Fundus examination was routinely done every 6 months to exclude diabetic retinopathy for all patients. Patients with suspected retinopathy were subjected to fundus photography to confirm diagnosis.

Quality of Life Assessment:

Assessment of health-related quality of life (HRQoL) was performed using the ***Pediatric Quality of Life Inventory Version 4.0 (Peds QL Generic Core Scale)***. It is a brief standardized assessment instrument developed by *Varni et al., 1999*. The Peds QL Generic Core scale systematically assesses patient's and parents' perception of HRQoL in pediatric patients with chronic health condition. It includes a physical summary scale (items assessing the child's functional status in activities of daily living) and psychosocial

summary scale (sum of emotional, social and school scales). Emotional scale assesses the child's emotional distress; social scale assesses interpersonal functioning in peer relations, while school scale assesses problems with cognitive performance and school attendance. The sum of the physical summary scale and the psychosocial summary scale is the total score.

The Pediatric Quality of Life Inventory Diabetes Module Version 3.0 (Peds QL Diabetes Diabetes Module) contains 4 modules: diabetes mellitus symptoms module, treatment anxiety module, worries module and communication module according to ***Varni et al., 2003.*** The sum of the four scales in the Peds QL Generic Core scale constitutes the total score. Each items has scores ranging from 0-4 (0 = It is never a problem, 1 = It is almost never a problem, 2 = It is sometimes a problem, 3 = It is often a problem, and 4 = It is almost always a problem). The higher the score, the poorer quality of life. Both inventories were translated into Arabic with blind back translation to English and the Arabic version was used.

Assessment of Emotional Status:

Emotional disturbances, specifically anxiety and depression, were assessed using Children's Manifest Anxiety (CMA) scale and Children Depression Inventory (CDI) for children above the age of 7 years. The CMA scale was designed by ***Abdel Hamid and El-Nail, 1991*** as an Arabic version derived from the children's manifest anxiety scale. This is a child self report measure that assesses symptoms of anxiety consisting of 36 statements with a total score of 0-36. The cut-off point of the scale is 18, where above 18, the child is considered to have high anxiety state.

On the other hand the Children Depression Inventory (CDI) was designed by ***Abdel Fatah(1989).*** It is an Arabic version developed from the children's manifest depression scale by *Maria Kovacas,* which was adapted from the well-known adult scale (The Beck Depression Inventory). The CDI is a 27 item –self report measure of mood symptoms in children.

Statistical Methods:

Analysis of data was done by IBM computer using SPSS (Statistical Program for Social Science) for chi-square test, unpaired t-test, correlation coefficient test and multi-variant analysis (linear regression). P value>0.05 was non-significant, *P<0.05 was significant, and **P<0.01 was highly significant.

Results

Table (1): Presents the main clinical and laboratory data of the studied patients and frequency of long-term diabetic complications. Diabetic retinopathy and neuropathy were diagnosed only in long-standing (group B) patients, while none of recently diagnosed patients experienced any of these complications. The mean glycosylated hemoglobin (HbA_1C) was significantly elevated in group (B) patients denoting poor glycemic control among the long standing diabetic patients. The test for microalbuminuria was repeatedly positive in 26% of group (B) patients compared to only 4.16% in group (A) indicating a significantly higher incidence of early nephropathy in long –standing diabetic patients.

Table (2) shows than 10 out of 14 patients with diabetic nephropathy (71.4%), as diagnosed by persistent microalbuminuria, were included among the poorly controlled group ($HbA_1C > 8.5\%$), and five of patients

with diabetic neuropathy and retinopathy (62.5% and 71.4% respectively) experienced poor diabetic control denoting a significant increase of diabetic microvascular complications in group III (poorly controlled) diabetic patients.

Table (3) shows a comparison between the three studied groups (according to the degree of glycemic control) regarding the scores of Peds QL Generic Core scale. It shows a significantly higher physical summary scale and emotional scale among group III patients (poorly-controlled) diabetic children denoting the worst quality of life, while the lowest mean score (best quality of life) was noticed in group II of them. The school performance scale was markedly increased (denoting a poor school performance) in group III followed by group I of patients. There was also a statistically highly significant difference between the studied groups regarding the psychosocial summary scale with the lowest mean (best quality of life) noticed in group II (fairly-controlled) diabetic patients. The total score was significantly elevated with a poor overall quality of life in group III (poorly-controlled) diabetic patients.

Table (4) shows that patients with poor glycemic control and diabetic microvascular complications, particularly those with longer disease duration, had the worst quality of life.

Table (5) shows a comparison between the three studied groups regarding the Peds QL Diabetic Module. The highest mean of diabetes symptoms module (worst quality of life) was noticed among group III (poorly-controlled) diabetic patients, while the treatment anxiety module was markedly elevated in group I patients with strict glycemic control. There was also a highly significant difference between the studied groups regarding the worry module scores with the lowest mean (best quality of life) in group II patients, and the highest mean (worst quality of life) in group III (poorly-controlled) diabetic patients.

Table (6) shows that depression and anxiety were common in our sample. As regards depression, the CDI showed a higher frequency of depression 31.6% in group III compared to 18.2% and 3.6% among groups I and II respectively, and the difference was statistically significant. When the three studied groups were compared as regards the mean scores of CDI, it was found that group III (the poorly-controlled) diabetic children had the highest scores of depression with a statistically significant difference from group II patients who had the lowest scores. The results regarding the presence of anxiety using the CMA revealed also a highly significant statistical difference between the three studied groups with a significantly higher frequency of anxiety (CMA scale > 18) in group III patients (73.3%) followed by group I (33.3%) and lastly group II patients (21.8%).

Table (1): Clinical and laboratory data of the studied patients

Parameter	Group (A) (DM < 5 years)	Group (B) (DM ≥ 5 years)	"p" value	Significance
Number Sex (M/F)	48 28/20 (1.4:1)	46 20/26 (0.77:1)	P > 0.05	Non – significant
Age (years), Mean ± SD	8.4 ± 2.5	14.2 ± 4.8	(t : 4.8) P < 0.001	Highly significant
Disease duration (years) Mean ± SD	2.3 ± 1.2	8.5 ± 3.8	(t: 8.0) P < 0.001	Highly significant
Mean blood glucose Mean ± SD (mg/dl)	180 ± 45.9	201 ± 55.4	t (0.66) P > 0.05	Non – significant
HbA_1C (%) Mean ± SD	8.04 ± 0.96	11.17 ± 3.74	t (2.1) P < 0.05	Significant
S. creatinine Mean ± SD (mg/dl)	0.7 ± 0.21	0.9 ± 0.32	t (1.1) P > 0.05	Non – significant
Creatinine clearance (ml/min/1.73m^2) mean ± SD	61.36 ± 13.57	40.2 ± 10.61	t (4.6) P < 0.01	Significant
Microalbuminuria (Qualitative) + ve test, (%)	2/48 (4.16%)	12/46 (26.08%)	t (8.0) P < 0.001	Highly significant
Diabetic retinopathy (number, %)	0/48 (0.0%)	7/46 (15.2%)		
Diabetic neuropathy (number, %)	0/48 (0.0%)	8/46 (17.4%)		

Table (2): Correlation study between glycemic control (according to HbA_1C) and diabetic microvascular complications

Diabetic Complication	Group	Degree of Glycemic Control			'p' value	Significance
		Good (I) no. = 24	Fair (II) no = 32	Poor (III) no = 38		
		No. (%)	No. (%)	No. (%)		
Nephropathy	- ve	23 (95.8)	29 (90.6)	28 (73.7)	P < 0.001	Highly significant
	+ ve	1 (4.2)	3 (9.4)	10 (26.3)		
Retinopathy	- ve	23 (95.8)	31 (96.88)	33 (86.84)	P < 0.001	Highly significant
	+ve	1 (4.2)	1 (3.12)	5 (13.16)		
Neuropathy	- ve	23 (95.8)	30 (93.75)	33 (86.84)	P < 0.001	Highly significant
	+ ve	1 (4.2)	2 (6.25)	5 (13.16)		

Table (3) Comparison between the three studied groups as regards the mean scores of Peds QL Generic Core scale version 4.0 (Child Report)

Scale	Mean ± SD	F	P value	Significance
Physical summary scale				
Group I (good control)	9.3 ± 4.3	6.1	0.003**	Highly significant (group II vs. group III)
Group II (fair control)	6.5 ± 4.3			
Group III (poor control)	10.5 ± 5.4			
Emotional scale				
Group I (good control)	7.7 ± 5.0	8.0	0.01* 0.001**	Highly significant (group I vs. group II) (group II vs. group III)
Group II (fair control)	4.1 ± 3.1			
Group III (poor control)	8.6 ± 4.7			
Social scale				
Group I (good control)	7.0 ± 4.7	2.3	0.1	Non significant
Group II (fair control)	4.5 ± 4.1			
Group III (poor control)	6.3 ± 4.6			
School performance scale				
Group I (good control)	6.5 ± 2.3	8.4	0.001**	Highly significant (group I vs. group III) (group II vs. group III)
Group II (fair control)	5.9 ± 3.8			
Group III (poor control)	10.4 ± 3.9			

Table (3) continued:

Scale	Mean ± SD	F	P value	Significance
Psychosocial summary scale				
Group I (good control)	22.0 ± 10.2	7.5	0.001**	Highly significant (group II vs. group III)
Group II (fair control)	15.4 ± 8.8			
Group III (poor control)	24.9 ± 10.4			
Total Score				
Group I (good control)	52.5 ± 14.8	8.3	0.001**	Highly significant (group II vs. group III)
Group II (fair control)	36.4 ± 12.6			
Group III (poor control)	60.7 ± 28.8			

Group I: Good control (HbA_1C: 6-7.5%), Group II: Fair control (HbA_1C:> 7.5- 8.5%), Group III: Poor control (HbA_1C > 8.5%)

****P< 0.05: Significant, ** P< 0.01: Highly significant P> 0.05: non significant***

Table (4): Correlation study between the total scores of Peds QL Generic Core scale and disease duration, diabetic microvascular complications and glycemic control

Parameter	Number (%)	Total Peds QL Score mean ± SD	'p' value	Significance
Sex Male	48 (51 %)	38.6 ± 22.4	> 0.05	Non- significant
Female	46 (49%)	44.8 ± 26.2		
Disease Duration				
< 5 years	48 (51%)	24.8 ± 19.2	< 0.001	Highly significant
≥ 5 years	46 (49%)	62.4 ± 38.6		
Glycemic control				
Good (group I)	24 (25.5%)	52.5 ± 14.8	< 0.001	Highly significant (Group II vs. III)
Fair (group II)	32 (34.0%)	36.4 ± 12.6		
Poor (group III)	38 (40.5%)	60.7 ± 28.8		
Nephropathy				
- ve	80 (14.9%)	36.4 ± 18.5	< 0.001	Highly significant
+ ve	14 (85.1%)	72.8 ± 26.3		
Retinopathy				
- ve	87 (92.55%)	38.1 ± 20.4	< 0.001	Highly significant
+ ve	7 (7.45%)	81.6 ± 22.8		
Neuropathy				
- ve	86 (91.5%)	37.2 ± 21.5	< 0.001	Highly significant
+ ve	8 (8.5%)	82.8 ± 28.9		

Table (5): Comparison between the three studied groups as regards the Peds QL Diabetes Module

Module Scale	Mean ± SD	F	P value	Significance
Diabetes symptoms module				
Group I (good control)	17.5 ± 9.2	3.8	0.02*	Significant (Group II vs. Group III)
Group II (fair control)	16.6 ± 7.2			
Group III (poor control)	21.1 ± 6.6			
Treatment anxiety module				
Group I (good control)	16.0 ± 8.2	5.8	0.01**	Highly significant (Group I vs. Group II)
Group II (fair control)	4.7 ± 3.1			
Group III (poor control)	8.6 ± 4.7			
Worry module				
Group I (good control)	7.3 ± 4.3	6.5	0.002**	Highly significant (Group I vs. Group II) (Group II vs. Group III)
Group II (fair control)	4.0 ± 3.7			
Group III (poor control)	8.9 ± 3.7			
Communications module				
Group I (good control)	6.5 ± 3.3	1.6	0.2	Non - significant
Group II (fair control)	5.7 ± 3.5			
Group III (poor control)	7.3 ± 4.4			

Table (6): The Child Depression Inventory (CDI) scores and Children Manifest Anxiety (CMA) in the studied groups

Children Depression Inventory (CDI) scores						
Group	**Mean ± SD**	**F**	**P value**	**Significance**		
Group I (good control)	9.0 ± 5.3	3.8	0.04*	Significant (Group II vs. III)		
Group II (fair control)	8.4 ± 4.2					
Group III (poor control)	12.2 ± 6.9					
Child Manifest Anxiety (CMA) scale						
Group	**Anxiety (+ ve > 18)**		**No anxiety (-ve ≤ 18)**		**X^2**	**P value**
	No.	**%**	**No.**	**%**		
Group I (good control)	8	33.3%	16	66.7%	14.3	0.001** Highly significant (Group I vs. III) (Group II. vs III)
Group II (fair control)	7	21.8 %	25	78.2%		
Group III (poor control)	28	73.7%	10	26.3%		

Discussion:

In this study, we attempted to assess health-related quality of life (HRQoL) and emotional disturbances in children and adolescents with type -1 diabetes mellitus (DM). The relation of HRQoL and emotional disturbances to glycemic control and microvascular diabetic complications was also studied. Patients of the present study were divided according to the degree of glycemic control (as reflected by HbA_1C levels) into well controlled (group I), fairly controlled (group II) and poorly controlled (group III) patients. Two scoring systems (the Peds QL Generic Core Scale and Peds QL Diabetes Module) were used as a comparative measure of quality of life among the three studied groups. The frequency and severity of anxiety and depressive symptoms were also studied and analysed using Children's Manifest Anxiety (CMA) Scale and Children Depression Inventory (CDI) respectively.

The results of the Peds QL Generic Core Scale revealed that the poorly controlled (group III) patients had the highest total score and thus, they experienced the worst quality of life, while the fairly controlled (group II) patients experienced the best quality of life, followed by the well controlled (group I) patients. Analysis of the subitems of the scale (physical, emotional, school performance and psychosocial summary scale) revealed similar significant higher scales in group III patients denoting marked impairment of quality of life through its all domains. Similarly, the results of the Peds QL Diabetes Module showed significantly higher scores (the worst quality of life) in the poorly controlled patients particularly for the worry module and diabetes symptoms module followed by the well controlled group.

In agreement with these Findings, *Wikby et al, 1993, Wikbald et al., 1996 Cameron et al., 2003 and Wagner, 2004* found that patients with poorly controlled DM had their physical and mental health lower than patients with good metabolic control. They added that patients with acceptable glycemic control without tight or strict dietetic restrictions experienced the best quality of life and least emotional disturbances, a similar result to that of the present study. The poor quality of life and more emotional disturbances in patients with poor glycemic control could be attributed to more frequent hospital admissions, shifting to more intensive insulin regimens as an attempt to correct underlying metabolic derangement, and the higher frequency of microvascular complications (nephropathy, retinopathy and neuropathy) in patients with poorly controlled diabetes. In a recent study done by *Salem et al, 2003* describing the impact of glycemic control on the quality of life in diabetic children and adolescents, they also found that the poorly controlled group experienced the worst quality of life, while the fairly controlled group had the best scores.

The finding that patients with well-controlled DM in the present study rated their quality of life poorer than the fairly controlled group with more emotional disturbances could be attributed to the use of more intensive insulin therapy with marked dietary restrictions which diminishes the possibility to act spontaneously. The frequent home testing for blood glucose and the repeated occurrence of hypoglycemic episodes with

intensive therapy will make the patient feels helpless and in need of others to deal with these events *(Cameron et al.,2003 Hahl et al., 20002 and Salem et al 2003)*.

Longer disease duration and presence of diabetic microvascular complications showed a negative impact on the quality of life of the studied patients (affecting both Peds QL Generic Core Scale and Peds QL Diabetes Module) with more frequent emotional disturbances regarding both anxiety and depression scales in patients with long-term diabetic microvascular complications (nephropathy, retinopathy and neuropathy). This comes in agreement with *Hahl et al., 2002* who studied the quality of life in diabetic Finnish children and adolescents, and its relations to age, sex, disease duration, glycemic control and long-term microvascular complications. They described a negative influence of increasing age and disease duration on the quality of life. Moreover, they reported that patients with long-term diabetic complication experienced the worst quality of life effecting all its domains (physical, emotional, social, and school performance scales), a similar finding to that of the present study. Another study done by *Cameron et al., 2003* proved that the psychological indices and the general well being were worse with increasing age and longer disease duration, specifically in the prepuberal and pubertal children and adolescents.

Regarding depression and anxiety scales, the present study showed that the poorly controlled diabetic patients had significant higher incidence of depression and anxiety in comparison to the other two groups. These findings add more strength to the results of the emotional subscale of the Peds QL Generic Core Scale and Peds QL Diabetes Module discussed before. The higher frequency of depression and anxiety in poorly controlled patients would not only add to their poor quality of life, but could make the control of diabetes more problematic as stated by *Andersson et al., 2003***.** Depression and anxiety may lead to the activation of hypothalamic- pituitary-adrenal axis leading to more hyperglycemia and resistance to treatment secondary to the effect of increasing levels of adrenal glucocorticoids which may end in refusal of treatment or non-compliance to therapy. *Laffel et al., 2003* added that the concern about long-term complications, coping with acute complications, and the burden of treatment regimen combine together to affect virtually all psychological domains of life in type -1 diabetic patients**.**

The findings of this study indicate the importance of proper glycemic control in diabetic children and adolescents in order to allow them to have the best quality of life with early detection of diabetic micro-vascular complications which may inversely affect the quality of life. This could be done through a balanced approach aiming for acceptable intermediate control so that, the intensive treatment, strict regime and the dietary restrictions would not affect the quality of life. Moreover, the present study highlights the importance of detecting psychological and emotional disturbances in diabetic children and adolescents with early intervention so as to avoid their impact on the control of diabetes and subsequently, a better quality of life will be achieved.

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Diagnostic Value of Regional Cerebral Blood Flow Changes on SPECT and Hippocampal Atrophy on MRI in Diagnosis of Alzheimer's Disease and Vascular Dementia

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Abstract:

This study was performed to evaluate the role of regional cerebral blood flow changes on ^{99m}Tc-HMPAO brain SPECT and hippocampal atrophy on MRI in diagnosis of Alzheimer's disease and vascular dementia. The study was performed at radiology department and Institute of Psychiatry, Faculty of Medicine, Ain Shams University and a private radiology center, at the period from December 2004 to November 2005. Ten patients with clinical diagnosis of Alzheimer's disease 10 patients with vascular dementia and 5 aged matched healthy control were included in the study. All subjects underwent MRI assessment of hippocampus and brain perfusion SPECT. Mean normal hippocampal volume was (1806.5mm^3 ± 197), mean volume at cases of AD was (1408mm^3 ± 143.5) and mean volume at cases of VaD was (1540mm^3 ± 74.9). Hippocampal atrophy was recorded in 80% of AD patients and 90% of VaD patients. SPECT study revealed predominant parieto-temporal hypoperfusion in AD patients, while heterogenous tracer uptake with foci of hypoperfusion allover the brain and frontal involvement was elicited in cases of VaD. Decrease hippocampal volume can be used as a marker of dementia without specification to its cause. However SPECT is more specific. Combined both modalities is an adjunct to cognitive and clinical examination in diagnosis and assessment of disease progression.

Introduction:

Alzheimer's disease (AD) and vascular dementia (VaD) are the two major diseases that cause dementia and early diagnosis and intervention are essential for effective treatment ***(Yoshikawa, et al. 2003)***. By the time AD or even mild cognitive impairment (MCI) are clinically detectable, an important neuronal loss has already taken place ***(Masdeu, et al. 2005).*** Although no currently available treatment has been proven to stabilize or reverse the neurodegenerative process, and no available preventive treatment, several putative disease modifying agents are now in development with early clinical trials. Primary targets of such interventions are people who are at risk or who are at mild to moderate stages of the disease to delay its progression ***(Kantarci & Jack 2003).***

In absence of a robust biological marker, the diagnosis relies largely on clinical features and requires a thorough neurological and neuropathological evaluation ***(Varma, et al 2002).***

Clinical diagnosis of AD in a living person is labeled either possible or probable. Definitive diagnosis of AD requires tissue examination, through biopsy or autopsy of the brain ***(Kantarci & Jack 2003)***. From the epidemiological point of view, it has become increasingly clear that the prevalence of VaD is heavily dependent upon the diagnostic criteria used and that, accordingly, a low level of agreement exists among different authors on how to diagnose

VaD ***(Verhey. et al. 1996, Wetterling, et al. 1996 & Chui et al 2000)***. In these studies the highest prevalence values have been obtained adopting the Hachinski ischemia scale ***(Hachinski et al. 1975)*** or the DSM-IV diagnostic criteria and the lowest values have been obtained with the NINDS-AIREN diagnostic criteria for VaD. ***(Roman et al 1993)***. In the same studies, the level of agreement (k coefficient) in making diagnosis of VaD has been consistently low (ranging between 25% and 60%), whereas a much higher agreement (80% - 90%) has been obtained in making a diagnosis of Alzheimer's disease (AD) ***(Gainotti 2004)***.

The disagreement between clinical and pathological diagnosis provides the motivation to develop neuroimaging markers that can accurately identify the different types of dementia pathology ***(Masdeu, et al. 2005)***.

The traditional use of structural neuroimaging to differentiate potentially reversible or modifiable causes of dementia such as brain tumors, subdural heamatoma, normal pressure hydrocephalus, and neurodegenerative diseases with focal atrophy, from AD is widely accepted ***(Knopman et al. 2001).*** Structural neuroimaging can also identify anatomic changes that occur from the pathologic involvement in AD. Neurofibrillary pathology, which correlates with neuron loss and cognitive decline in patients with AD, initially involves the primary sensory cortices. The macroscopic result is atrophy. For this reason, the search for anatomic imaging markers of AD has targeted the anteromedial temporal lobe, particularly the hippocampus and entorhinal cortex which are involved earliest and most severely in AD ***(Kantarci & Jack 2003)***. Rate of atrophy of entorhinal cortex (ERC) have been reported to be larger than that of hippocampus. However, technical issues and sometimes ambiguous landmarks to define structural boundaries make ERC measurement less reliable than that of hippocampus ***(Du et al. 2004).*** Overall brain volume loss, although not specific, has also been reported as a hallmark of AD showing correlation with disease severity ***(Chan et al. 2003).*** The intimate correlation between pathologic involvement and hippocampal atrophy is encouraging for the use of hippocampal volumetery, using MRI, as an imaging marker and a diagnostic criterion of the disease ***(Knopman et al. 2001 & Kubota et al. 2005).*** Also ***Gainotti and coworkers 2004***, investigated the role of hippocampal atrophy in assessing the severity of dementia in patient with vascular disease.

Previous workers have suggested that a combination of both functional and anatomic imaging studies may offer better sensitivity and specificity for the diagnosis of AD ***(Varma et al 2002).*** SPECT and PET are widely investigated functional neuroimaging techniques which evaluate global and regional disturbances of blood flow and metabolism, and helps improving our understanding of pathophysiology of dementing illnesses ***(Lee et al. 2003).*** As perfusion SPECT is less expensive and more available than FDG PET, the study we present here examines the diagnostic utility of abnormalities of cerebral blood flow (CBF) as demonstrated by ^{99m}Tc-HMPAO and hippocampal atrophy demonstrated by MRI as diagnostic indicators of dementia in patients with AD and VaD.

Patients and Methods:

This study was conducted at radiology department and Institute of Psychiatry,

Faculty of medicine Ain Shams University and a private radiology center, at the period from December 2004 to November 2005. Twenty patients were included in the study, as shown in table (1) 10 patients (4 males and 6 females) fulfilled the criteria AD and 10 patients (3 males and 7 females) fulfilled the criteria for VaD according to ICD-10 respectively. The mean age of the patient with AD was 62.8±7.34 with a mean duration of illness 2.95±4.81 while the mean age of patient with VaD was 64.5±6.21 and mean duration with illness 3.6±5.57. All patients were diagnosed clinically using the ICD-10 symptoms checklist after a complete neuropsychiatric examination. Moreover patients with VaD were subjected to Hachinski ischemic scale to verify the diagnosis as well as assessment of the previous radiological findings of the CT or MRI

Also 5 aged matched healthy control were involved in the study; they had no history of neurological or psychiatric disorders or major medical illness, with normal neuropsychiatric examination. All patients or the relatives and control group gave their consent prior to the study.

Patients were excluded from the study when other neurological and non neurological disorders were detected. All patients and control group were right handed.

Brain perfusion SPECT and MRI evaluation of the hippocampus volume were performed in all subjects.

MRI scanning:

We used Philips Intra 1.5T MRI scanner with a head coil and patient in supine position. The method of calculating the hippocampus volume was used after ***Bremner et al, 1995*** An initial sagittal T1 localizing sequence (TR=572, TE= 15) was obtained to determine the long axis of the hippocampus **(fig 1).** Coronal sections were obtained perpendicular to the long axis of the hippocampus with slice thickness = 3mm and 1 mm space. On the work station, we used an oval shape region of interest (ROI), placed around the outline of the hippocampus in each coronal section **(fig2),** with intent to achieve maximum coverage and to get surface area for each slice. Then by soft ware assessment the volume is automatically calculated for each hippocampus. By summation of the Rt. And Lt. Hippocampus volumes and dividing by 2 we got the mean hippocampal volume for each participant.

SPECT Scanning:

Brain SPECT was done using ^{99m}Tc-HMPAO (technetium ^{99m} labeled hexamethyl propylene amine oxime) in a dose of 20mCi injected intravenous. Patient data were acquired and reconstructed using a FUFA-SMV-DSTXLi digital gamma camera machine. Energy window 10% centered over the 140 kev peak. Imaging time is 20 minutes after injection. Acquisition protocol is 30 minutes using an annular SPECT system, 360 degrees, 120 images, 15 sec/image, matrix size128x128 1 byte per pixel. Patient was supine, with the head slightly elevated and eyes closed. Patient's head should be as close as possible to the camera and strapped tightly with a non attenuating object (rubber) to avoid head motion. Axial, sagittal and coronal projections were obtained.

Analysis of the data obtained from SPECT and MRI studies were done with 3 expert radiologists and correlations with clinical condition were done.

Results:

MRI findings:

The mean normal volume of the hippocampus was (1806.5 mm^3 ± 197); however the mean volume recorded in patients with AD was (1408mm^3±143.5) and in patients with VaD was (1540mm^3 ± 74.9). Two cases of AD showed normal hippocampal volume (mean 1796.2mm^3) and they also had mild cognitive impairment and short duration of the disease (mean 1.25years). Sever hippocampal volume loss was detected in 4 patients with the mean volume of hippocampus was (1064 mm^3 ± 44.6). Three patients of VaD showed marked decrease in hippocampal volume with mean volume (1256mm^3± 22.5). While one patient showed normal hippocampal volume (1708 $mm^{3)}$. (**Table 2)**.

SPECT findings:

All cases of AD and VaD showed heterogenous tracer uptake with areas of hypoperfusion (**table 3)**. Prominent parieto-temporal decrease tracer uptake was seen in 8 cases of clinically diagnosed AD **(fig 3).** While heterogenous hypoperfusion allover the brain was seen in two cases, one of which had normal hippocampal volume in MRI (1786.3mm3) **(fig 4).** Radiological findings were more consistent with VaD.

Heterogenous areas of decrease tracer uptake were seen in 9 cases of VaD with small foci of hypoperfusion allover brain lobes involving the frontal lob one **(fig 5)**. However one case showed predominant parieto-temporal hypoperfusion **(fig 6)** and MRI findings revealed marked decrease hippocampal volume (1045.8mm3). Radiological findings were more suggestive of AD

Two of the control subjects (none dementing) showed areas of hypoperfusion at parietal lobes. **(fig 7).**

Table (1):Characteristic of the Sample:

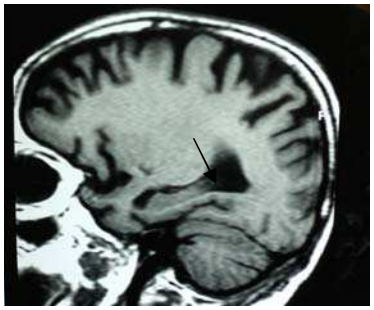
Group	Mean age in years ± SD	Sex		Mean duration of the disease in years ± SD
		Male	Female	
AD	62.8±7.34	4	6	2.95±4.84
VaD	64.5±6.21	3	7	3.6±5.57
Control	62.2±7.67	3	2	-

Table (2): Mean hippocampal volume recorded at included subjects:

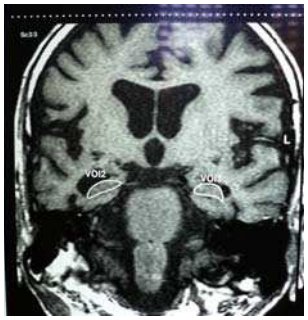
	AD	VaD	Normal
Mean hippocamal volume in mm3± SD	1408±143.5	1540±74.9	1806.5±197

Table (3): SPECT and MRI findings in correlation with clinical diagnosis:

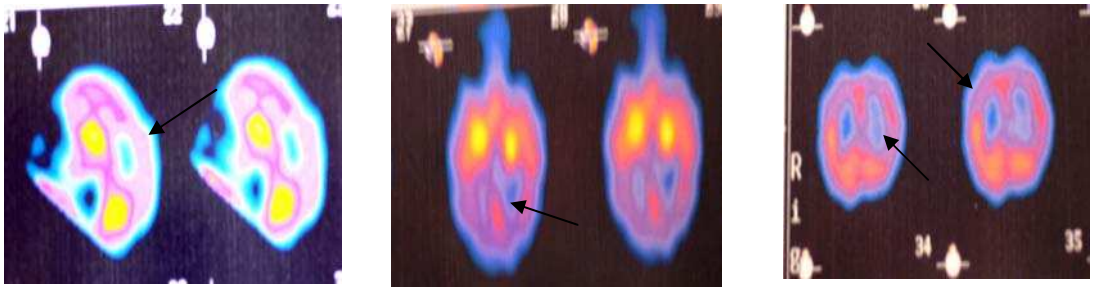
Findings	AD N=10	VaD N=10	Control N=5
Brain SPECT			
Heterogenous hypoperfusion ± frontal involvement	2	9	0
Parietal / temporal hypoperfusion	8	1	2
Normal perfusion	0	0	3
Hippocampal volume			
Decrease	8	9	0
Normal	2	1	5



Fig(1): T_1 sagittal localizing MRI shows long axis of the hippocampus the hippocampal body

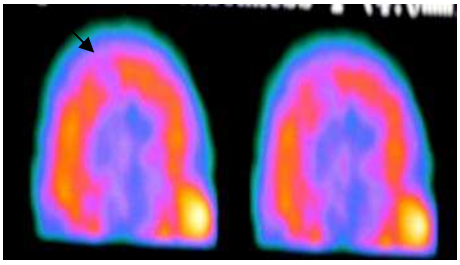


Fig(2): coronal T1 MRI shows an oval region of interest outlining



A P C

Fig(3): Brain SPECT of AD patient (A: Sagittal, B: Axial and C: Coronal) shows predominant parieto-temporal hypo-perfusion.


A

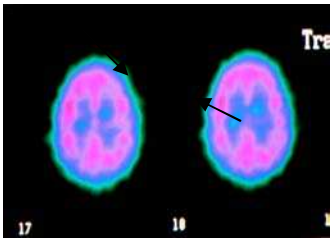
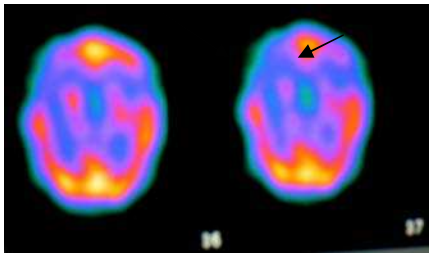
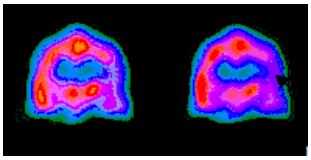

B

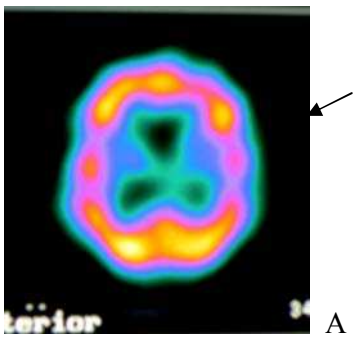
Fig (4): Brain SPECT (A: Sagittal and B: Axial) shows heterogenous tracer uptake allover the brain(arrows) in a case clinically diagnosed as AD, MRI of this case shows normal hippocampal volume



Fig(5): Brain SPECT (axial) in a patient with VaD shows hypo-perfusion of the frontal lobes.



Fig(6): Brain SPECT (coronal)of a clinically diagnosed VaD patient shows areas of hypo-perfusion at tempero-parietal lobe.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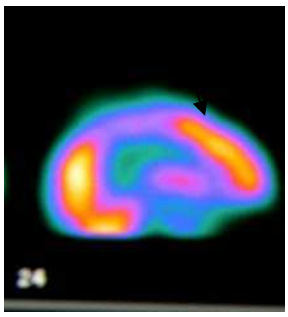
B

Fig(7): Brain SPECT (A:axial and B:sagittal) of a normal individual shows areas of hypo-perfusion at parietal lobes.

Discussion:

When elderly patient presents with cognitive impairment, the clinical distinctions to be made are: first between ages related decline and dementia, second (if dementia is established) between different etiologic types.

Alzheimer's disease (AD) is the most common cause of dementia and accurate diagnosis is important for effective treatment. While clinical criteria for the diagnosis of AD have been substantially important, they are still imperfect, and imaging findings change the clinical diagnosis and management in some cases ***(Roman et al. 1993).***

Risk groups for AD are composed of individuals identified either through clinical examination or family history and genetic testing. They are the primary targets of treatment trials aimed to prevent or delay the neurodegenerative process. Thus biomarkers that can distinguish individuals at risk are required to use these interventions before neurodegenerative disease advances and irreversible damage occurs ***(Kantarci and Jack 2003).***

Functional imaging using photon emission tomography (PET) scanning has shown reduction in cerebral metabolism and blood flow in AD, predominantly in posterior parietal and temporal region but the method is too costly for routine clinical use. The regional uptake of ^{99m}T-HMPAO into the brain as measured by single photon emission computerized tomography (SPECT) provides a quantitative representation of regional cerebral blood flow and requires a rotating Gamma camera of the type found in most nuclear medicine departments and relatively inexpensive ***(Mckeith et al. 1993).***

MRI commonly demonstrates three types of abnormalities in patients with dementing disease. First lacunar infarctions that provide evidence of cerebrovascular disease and are common in VaD than other types of dementia. Secondly, areas of high signal on T2 weighted MRI, are commonly seen in patients with dementia. The third abnormality seen on MRI is accelerated atrophy compared with normal elderly individuals. More over, the distribution and rate of atrophy differ depending on the disease process ***(Varma et al 2002).*** **Zarow et al, 2005 stated** that although brain atrophy per se is not specific to dementia of Alzheimer's type, there is strong evidence suggesting that rate of atrophy of certain brain structures are correlated with AD severity. In particular, atrophy of hippocampus occurs early in the development of the disease and has been reported to correlate with deficits in memory function. Also other workers have found that measurement of hippocampal volume or cross sectional area can distinguish patients with AD from normal individuals and from patients with other neurodegenerative diseases with specificity of over 95% ***(O'Brien et al. 1997).***

The aim of this study is to evaluate the role of regional atrophy on MRI (represented by hippocampal volume) and cerebral blood flow changes on SPECT in differentiation between the two most common causes of dementia, that are AD and VaD. We provided data on how useful individual imaging findings are (in isolation and in combination), and serve as a guide to the optimal use of neuroimaging in the clinical diagnosis of dementia.

The results of our study revealed that hippocampal atrophy is detected in 80% of

AD and 90% of VaD. This is consistent with ***(Hanyu et al. 1999)*** who reported that hippocampal atrophy is not specific marker for AD and appears to be a common phenomenon in dementia syndrome. More over ***Gianotti et al 2004*** reported that hippocampal atropy is a better predictor of dementia than the number of the vascular lesion in patients with multiple subcortical infarcts. Similar results with ***Henon et al 1998 & Fein et al 2000*** who found that in patients with subcortical ischemic vascular lesion, dementia correlates best with hippocampal and cortical atrophy than with any measure of lacunae. However; ***Du et al 2002*** fount that the entrohinal cortex and hippocampus are less affected by vascular dementia that AD. The limited number of our patients in this sample may be the cause of this disagreement.

Therefore the controversial results of the hippocampal atrophy lead the investigators to use the entrohinal (ERH) cortex in addition as a way to differentiate between different types of dementia however it was found that (ERH) volume loss is also present in Alzheimer's disease and fronto-temporal dementia. However ***Masdeu et al 2005*** reported that the annual rate of volume change has a greater sensitivity and specificity than one time measurement.

In our study brain SPECT examination, heterogenous cerebral blood hypo-perfusion was revealed in all cases of AD and VaD in comparison to normal group. However the distribution of tracer uptake was different between AD and VaD patients. In 80% of AD cases there was a variable degree of decrease perfusion mainly at posterior cortex, involving the temporal and parietal regions. No specific pattern of defective cerebral blood perfusion was seen at cases of VaD. The most predominant pattern was heterogenous hypoperfusion with scattered areas of decrease tracer uptake seen at frontal, parietal and occipital regions, only one case shows parietotemporal hypoperfusion and radiological diagnosis was in favor of AD. Involvement of frontal cortex was absent in all cases of AD.

Our study is consistent with ***(ElFakhri et al., 2003)*** and previous reports that confirmed the presence of perfusion abnormalities in patients with established AD. The most consistent finding in these studies was decrease perfusion in the tempro-parietal cortex. Another study done by ***(Varma et al., 1997)*** using ^{99m}Tc-HMPAO, confirmed the presence of bilateral posterior cortical blood flow abnormality in cases of AD but they did not find a pattern of reduced cerebral blood flow in SPECT of value in the diagnosis of VaD.

Also ***Yoshikawa et al., 2003*** using ^{99m}Tc-HMPAO with 3D fractal analysis (statistical imaging processing on reconstructed data). They divided the whole brain into anterior and posterior regions in patients with AD and VaD, fractal dimension was calculated for each region. The results were: posterior predominant heterogeneity of cerebral blood flow in the AD group and anterior predominant heterogeneity in VaD group.

Masdeu, et al. 2005 concluded that a positive SPECT increases the probability of diagnosis of AD to 92%, while a negative SPECT lowers this figure to 70%. While **Julin, 1997** have suggested that a combination of MRI and SPECT findings can provide excellent discrimination reaching 100% between AD and normal control. We can add that according to our results combined MRI and SPECT can help

in better differentiation between AD and VaD.

Recent radiological techniques has been used trying to differentiate between AD and VaD. **Masdeu, et al. 2005** comparing PET and SPECT found that PET is slightly more sensitive and specific than SPECT for the diagnosis of mild AD, but it is clearly better for the differential diagnosis of vascular dementia. Moreover, among several regions in the temporal lobe, reduced hippocampal volume on MRI and hippocampal glucose metabolism on PET were the best discriminators of patients liable to develop AD ***(Desanti et al. 2001).***

However, Recent studies using proton magnetic resonance spectroscopy (^{1}H MRS) have shown reduction of NAA (N-acetylaspartate) level in all lobes of the human AD brain especially temporoparietal and occipital lobes that shows a reduction of an approximately 15% . Another significant finding is the elevation of myo-inositol (MI) levels in the gray matter of AD brain ***(Kantarci et al. 2000).***

In conclusion, neuroimaging has the potential to play a large role in diagnosis of AD and its discrimination from other causes of dementia. There is strong evidence that imaging biomarkers are an adjunct to cognitive and clinical examination in diagnosis and assessment of disease progression. Decrease volume of hippocampus can be used as a marker of dementia without specification to the cause. Although most studies confirmed a relation of diminished hippocampal volume and AD, our study found significant decrease in the size of hippocampus in cases of VaD as well, SPECT study of brain blood perfusion revealed posterior predominant decrease perfusion in AD. While, heterogenous hypoperfusion with frontal lobe involvement was more predominant in VaD. Combined MRI and brain SPECT provides better diagnosis and differentiation of both diseases.

We advise to extend the scale of this study in the future to involve a larger sample volume and to study the reliability of these modalities in prediction of patients at risk to develop dementia.

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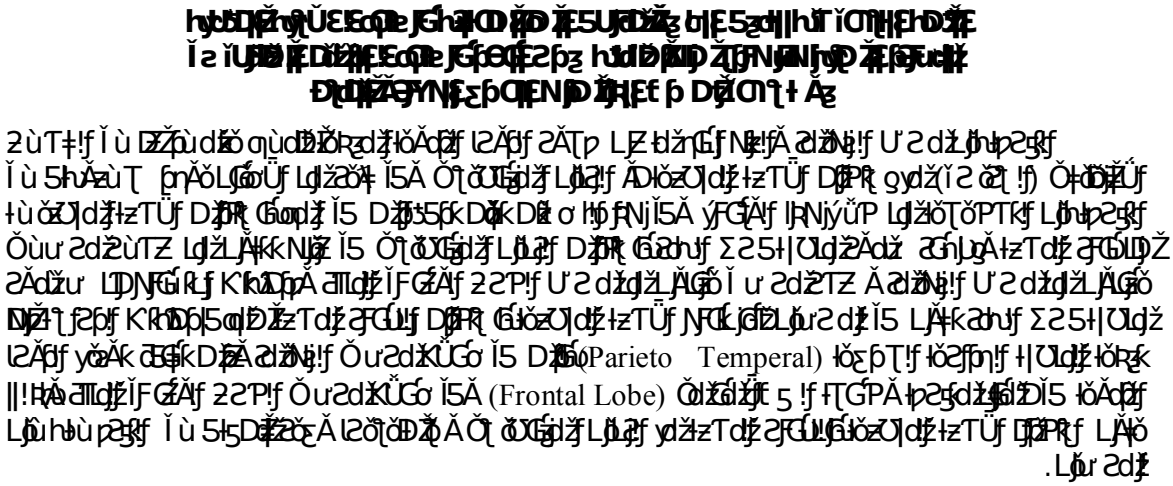


The Practice of Electroconvulsive Therapy (ECT) in a Sample of Egyptian Patients

Okasha T.

Abstract

Since its inception in 1938, ECT has proved effective and even life saving in certain psychiatric conditions when other treatments have been of little or no benefit. ECT is the only treatment in psychiatry that has withstood the test of time for nearly 70 years. ECT in Egypt is used in patients suffering from depression, mania, schizophrenia and catatonia which are slightly different from the literature where ECT is mainly used for depression; however, recently an abundance of literature has proved that ECT is as effective in mania as it is effective in depression. This study was carried out on 544 patients admitted to the Psychiatric Health Resort in New Cairo over a period of one year. From the 399 patients receiving ECT 273 (68%) were male and 126 (32%) were females. The 399 patients in this study received a total of 2866 ECT sessions. From these 2866 ECT sessions, 2734 sessions (95%) were given bilaterally and 132 sessions (5%) were given unilaterally. All psychiatrists should be acquainted with ECT and be able to present the treatment to the patient and the patient's relatives in a knowledgeable and scientific manner, in order to reduce the stigma and transmit the fact that it is no longer "shock" or "convulsive" treatment. Emphasis also should be that it is not a last resort treatment, but rather a first line therapy when indicated. An urgent goal of mental health care should be to provide access to ECT and eliminate the severe impediments to its use, so long as it can defend evidence based superiority over other treatments.

Introduction

This year the world celebrates 67 years of electro-convulsive therapy (ECT). There has been no other line of treatment in medicine that withstood the test of time for nearly six decades like ECT. The controversy over ECT is what enabled it to prove itself and helped it in its development to our present day as when a thing ceases to be a subject of controversy; it ceases to be a subject of interest.

Since its inception ECT has proved effective and even life saving in certain psychiatric conditions when other treatments have been of little or no benefit.

ECT was initially used to treat psychotic patients in whom schizophrenia was diagnosed. However, practitioners quickly began to discover that ECT was also useful in other psychiatric disorders mainly severe depression.

The stigma of ECT is one of the main issues that need to be addressed worldwide, ECT is a technically advanced and effective treatment that is often misunderstood and maligned by the lay public and by psychiatrists as well. From 1938 to the 1950's an extensive use of ECT was seen. During that period of time, ECT was the major treatment, if not frequently the only biological treatment available for mental illness (Fink, 1992).

From the 1950's through the 1970's with the advent of psychotropic medications (including the development of neuroleptics and of tricyclic antidepressants), a decline in the use of ECT was seen. In the 1970's,

concern developed regarding the side effects of psychotropic medications, including the cardiovascular effects of the tricyclic antidepressants and the potential for tardive dyskinesia with neuroleptics. This concern resulted in a resurgence of interest in ECT and led to many studies and reports evaluating the effectiveness of this modality.

At the same time, the myths, misinformation, and public outcry continued. Senator Eagleton lost his vice presidential bid when he revealed that he had received ECT. In the film "One Flew over the Cuckoo's Nest", Jack Nicholson portrayed a patient receiving ECT for the wrong purpose (coercion) and in the wrong fashion (without anaesthesia or muscle relaxant). While public concern continues as a result of negative media portrayal, progress in ECT has continued with significant medical advancements (Hay, 1992). Currently, there is a surge in ECT research and publications which has helped ECT to enter the biological age of psychiatry. A journal now is available only for research in ECT and allied sciences on a quarterly basis.

The semantic issue becomes paramount. It is very inappropriate to call such treatment "Shock therapy". Fink (1979 and Ottosson 2004) has pointed out that "Shock" has a specific meaning: it is the perception of the passage of an electric current. This produces pain and discomfort. The word "Shock" denotes perceptions that do not occur under anaesthesia. This would be analogous to labelling surgery "pain therapy".

This outdated use of language leads to negative attitudes and prejudice. The words "convulsion" and "seizure" both have special meanings to the public. Convulsions as portrayed by the mass media do not occur with modern ECT methods. "Seizure" is used in its' technical sense to refer to the patterned electrical response produced by an electrical stimulus on an EEG level.

Lack of awareness of the natural history of disorders treated by ECT in the Egyptian population make nearly 70% of families of patients believe that ECT is addictive and once they receive ECT they will continue to relapse and never get better unless they receive another course of ECT (Okasha, 2006).

The treatment itself should be given a new name that describes what is done in neutral, "unloaded" language. Words like "Shock", "Seizure" and "Convulsive" should be eliminated. Several proposed terms as "cerebroversion", analogous with "cardioversion", or "Central Stimulation" or "Central Stimulation with Patterned Response" (CSPR), in Egypt a proposal by Okasha (1988) suggested the use of "Brain Synchronization Therapy" (BST) or "Rhythm Restoration Therapy" suggested by Rakhawy (1982) all would be effective in correcting the semantic description of ECT.

Previous refusal and stigma have changed and decreased after the introduction of these new names to some university hospitals in Egypt, and families were more accepting of this treatment after they previously said that our patient can be admitted to hospital, but do not give him electric treatment.

The aim of this work is to review the practice of ECT in a selective Egyptian sample of inpatients and assess the mortality, complications and outcome of patients.

Subject and Method

The study was carried out as a retrospective descriptive study. Studying the files and retrieving the data of 544 patients admitted to the Psychiatric Health Resort in New Cairo over a period of one year. The psychiatric health resort is a private psychiatric hospital with both inpatient and out patient facilities.

Any patient receiving ECT was viewed regarding their sex, diagnosis and method of receiving ECT. All patients were included and the only exclusion criterion was not receiving ECT. All diagnoses were made according to the ICD-10 Research and Diagnostic Criteria (1993) using the ICD-10 symptom checklist (1994).

An informed consent was taken from all the patients or their relatives to be included in this study.

Patients receiving ECT were investigated routinely by complete blood count (CBC), erythrocyte sedimentation rate (ESR), fasting blood sugar (FBS), liver and kidney functions and ECG. Patients were fasting for a period of at least 6 hours before receiving the treatment. ECT was given three times weekly, bilaterally using the bitemporal electrode placement and unilaterally using d'Elia (1970) position.

Patients were given thiopental sodium and atropine by the IV route followed by succinyl choline and oxygenation. A Thymatron DG apparatus was used setting the energy dial according to age giving a charge of 100.8 - 277.2 millicolombs, a current of 0.9 ampere, a frequency of 30 - 50 HZ, a pulse width of 1.0 msec and a duration of stimulus of 1.87 - 2.20 seconds. The seizure was monitored by one channel of EEG and one channel of EMG. All seizures fulfilled the criteria for an effective seizure.

The criteria for an effective monitored seizure are:

- A post-ictal suppression index above 70 % (Weiner, 1991).

- A seizure concordance index above 50 % (Swartz and Larson, 1986).

- A seizure energy index above 550 units (Abrams, 1992).

Results

Out of the 544 patients admitted to the Psychiatric Health Resort over a period of one year, 399 patients received ECT. The oldest patient receiving ECT was 83 years old and the youngest was 18 years old. The distribution of patient' age can be seen in Table (1). This table should act as an eye-opener that elderly people who respond to ECT better than pharmacotherapy are deprived of this treatment due to the reluctance of the attending psychiatrists to prescribe it form fear of stigma. More education is needed to correct these wrong perception both for psychiatrists, patients and their families.

From the 399 patients receiving ECT 273 (68%) were male and 126 (32%) were females as shown in figure (1).

The patients were diagnosed according to the ICD10 research and diagnostic criteria using the ICD 10 symptom checklist. The diagnoses of the patients were as shown in figure (2). 166 patients (42%) were suffering from schizophrenia, 105 patients (27%) were suffering from bipolar disorder (mania), 63 patients (16%) were suffering from depression and 60 patients (15%) were suffering from other diagnoses.

The other diagnoses for the 60 patients included 13 patients with obsessive compulsive disorder, 32 patients with mental and behavioural disorder secondary to substance abuse, 1 patient with generalised anxiety disorder, 11 patients with personality disorder, 1 patient with panic disorder and 2 patients with somatization disorder (figure 3).

All patients with the label other diagnoses had co-morbid depression except for 8 patients from mental and behavioural disorder secondary to substance abuse group who had substance induced psychosis.

The 399 patients in this study received a total of 2866 ECT sessions. From these 2866 ECT sessions as shown in figure (4), 2734 sessions (95%) were given bilaterally using the bitemporal electrode placement position and 132 sessions (5%) were given unilaterally on the non dominant hemisphere using the d'Elia position (2.5 cms from the vertex of the head).

The patients receiving unilateral ECT had different diagnoses according to the ICD 10 as shown in figure (5). 10 patients (39%) were diagnosed with severe depression, 7 patients (27%) were diagnosed with bipolar disorder (mania), 5 patients (19%) were diagnosed with schizophrenia and 4 patients (15%) were diagnosed as other diagnoses who suffered from co-morbid depression. From the 132 patients receiving unilateral ECT 101 patients (77%) were above the age of 50 years and 31 patients (23%) were between the ages of 20 and 49 years.

Unilateral ECT was given to the patients for 3 reasons; firstly, some patients had exams and the need to decrease the cognitive deficit especially to recent memory was necessary, secondly some patients ran their own businesses and needed be supervising their work while hospitalized and thirdly some patients from the older age bracket were suffering from early cognitive decline.

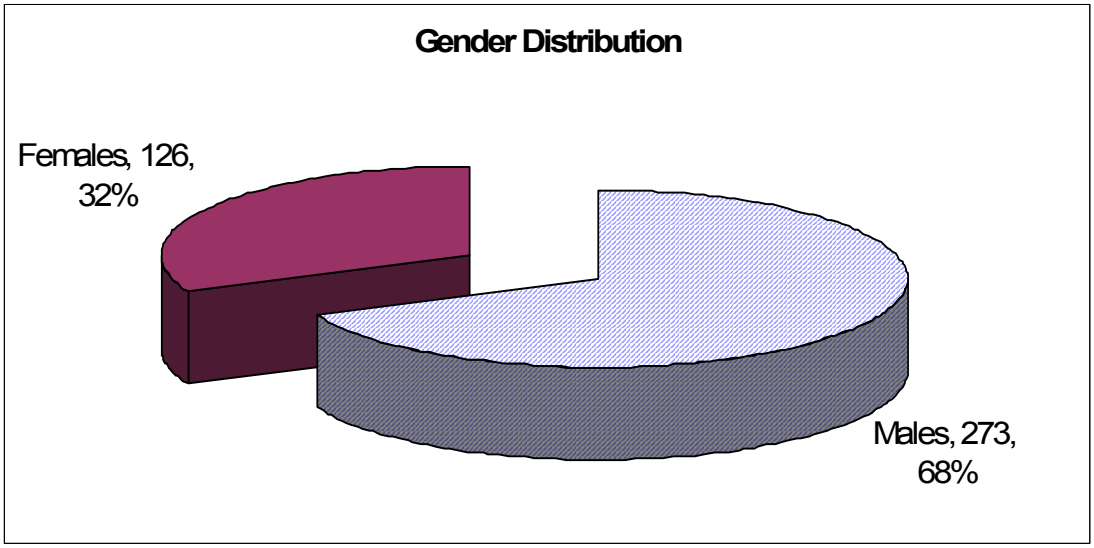
Out of the 2866 ECT sessions, as reported in the patient files, there were no mortalities, fractures or dislocations, specific complications whether cardiovascular or respiratory, or acute confusion states after the ECT sessions.

Upon discharge patients with depression showed an 80% improvement from admission, 85% improvement from admission in bipolar patients, 70% improvement from admission in patients with schizophrenia and 60% improvement in the category of patients diagnosed as other diagnoses. This improvement was evaluated comparing the on admission and on discharge Clinical Global Impression Scale (Severity).

Table (1). Distribution of patients by age

Age	Number of Patients
Below 20	17
21 - 30	129
31 – 40	111
41 – 50	71
51 – 60	33
61 – 70	22
Above 70	16

Figure (1)



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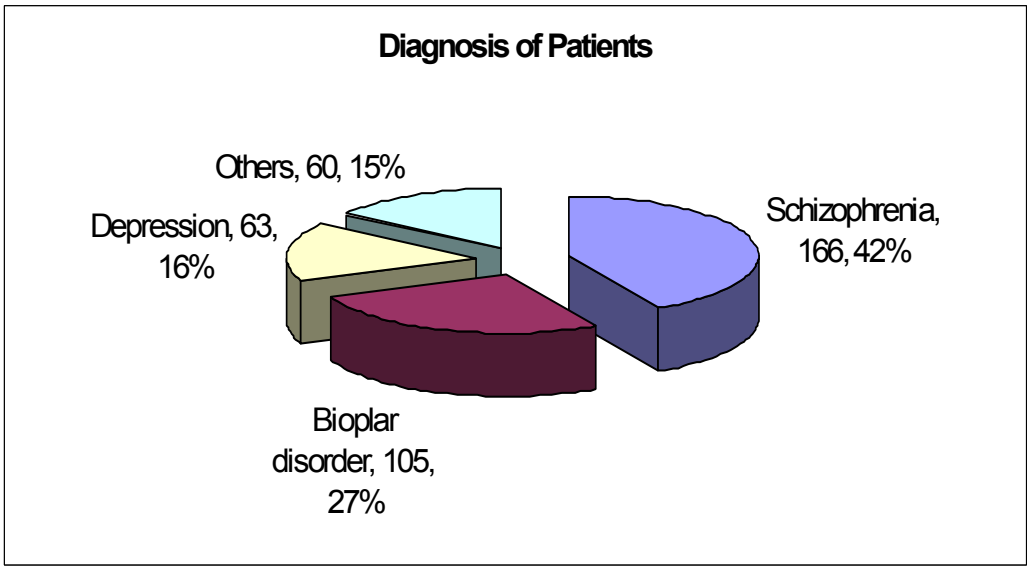

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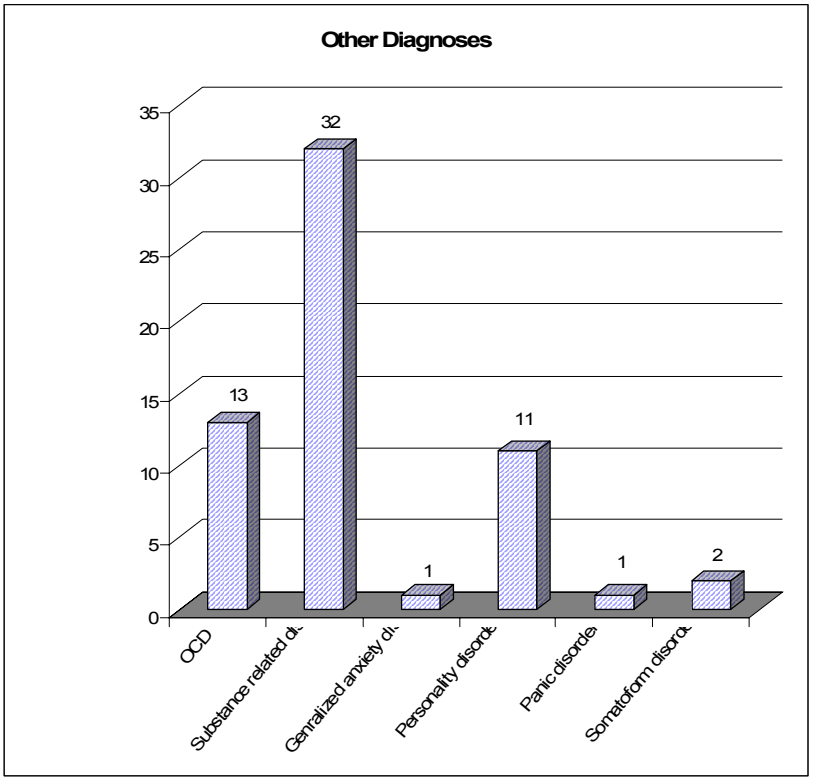


Figure (4)

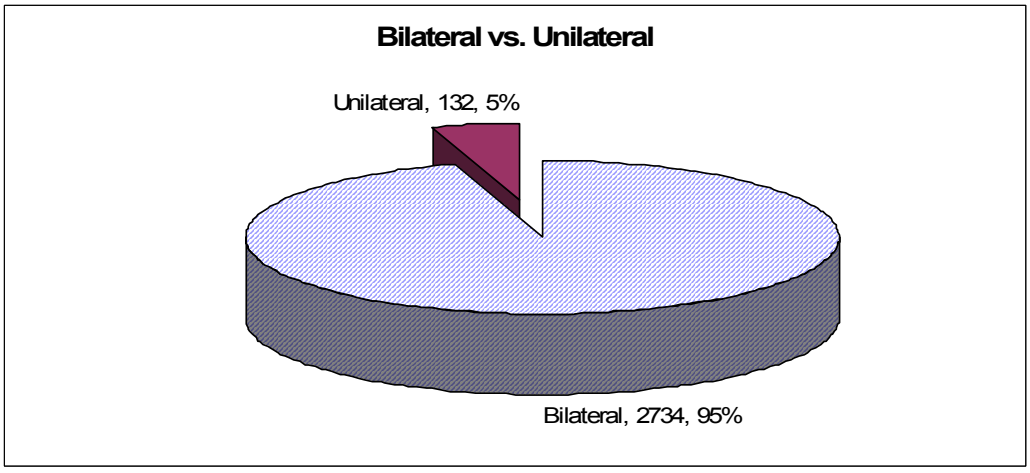
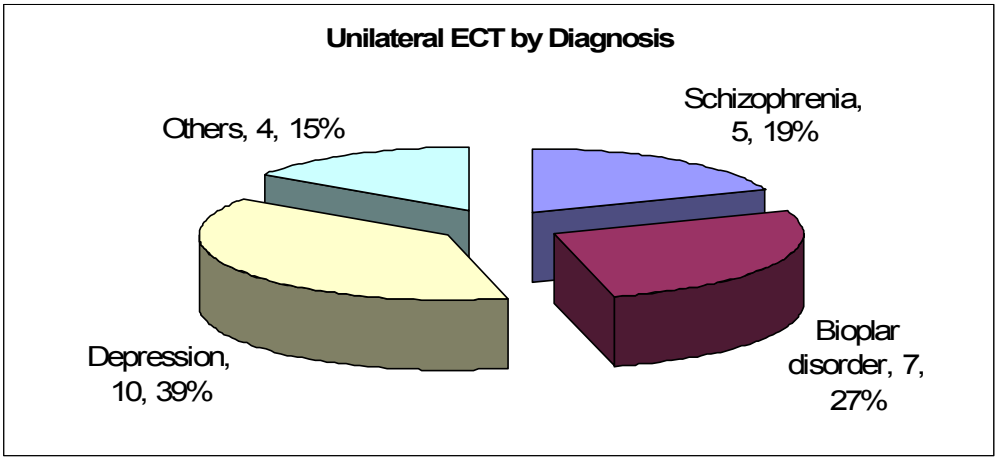


Figure (5)



Discussion

In this study, is to review the practice of ECT in a selective Egyptian sample of inpatients and assess the mortality, complications and outcome of patients.

Some countries like the United States and countries in Europe are reluctant to use ECT despite the evidence of the efficacy of this treatment. ECT was used in patients suffering from depression, mania and schizophrenia which are slightly different from the literature where ECT is mainly used for depression as reported by the Royal College of Psychiatrists (1995). However, recently an abundance of literature has proved that ECT is as effective in mania as it is effective in depression (American Psychiatric Association (2002). The American Psychiatric Association task force on ECT (2001), reported that ECT was underused and that there are many indications for ECT other than mood disorders and schizophrenia.

Out of the 399 patients 273 were male 126 female, the lower rate of female patients is consistent with the culture in Egypt and most developing countries where families prefer not to admit female patients for fear of stigma or because it might jeopardise their chances of getting married.

Many treatment algorithms developed over the years stated that ECT was used as last resort treatment for patients who were not responding to pharmacotherapy or psychotherapy. Recently all these algorithms state the efficacy of ECT and the importance of using it patients to reach faster response and allow our patients to have a better quality of life.

Egypt and most developing countries have many economic and financial problems which necessitate finding a treatment which has a rapid onset of action, shorter duration of stay in hospital, leads to the use of lower doses of pharmacotherapy and is cheap compared to the newer generations of antipsychotics and antidepressants. ECT is one of the main answers.

In a study conducted in Egypt by Okasha and Ramy (2006) to review the economical

aspects of using ECT in mania, carried out on 60 patients in both a university hospital and a private psychiatric hospital, it was found that patients receiving ECT for the treatment of mania compared to patients not receiving ECT had a shorter hospital stay at 19 days versus 38 days and the cost of hospitalization was 4845 EGP (850 USD) compared to 8464 EGP (1485 USD) in the non ECT group. The cost of treatment as well as the duration of stay in hospital are critical factors in psychiatric health care in Egypt, where the turn over is high in hospitals in order to accommodate patients in need for hospitalization and at the same time decreasing the cost of hospitalization, which is essential due to budget constraints, noting that unfortunately, the majority of patients pay for these services out of their pockets in Egypt.

Similarly the use of ECT in patients with co-morbid severe depression with other axis I diagnoses such as OCD, panic and substance abuse was effective in the alleviation of depression and improving the symptoms of the primary diagnosis with pharmacotherapy, this does not mean that ECT should be used as a first line treatment for these disorders.

From the 2866 ECT sessions there were no mortalities which are in agreement with the literature which states that the mortality rate with ECT is 1/10000 ECT sessions (Royal College of Psychiatrists, 1995). There were also no cardiovascular or respiratory complications or acute confusion states which are common with the use of non-modified ECT (Beyer etal., 1998).

The group of patients receiving unilateral ECT was in an attempt to decrease the cognitive deficit that patients may suffer with bilateral ECT mainly as recent memory affection.

Developing countries should not follow the steps of developed countries when it comes to algorithms in treatments, but should create their own guidelines for treatment which in more reality based according to their needs and economical situation. It should be the first line treatment for severe depression (psychotic depression), acute mania and excited or agitated schizophrenia.

All psychiatrists should be acquainted with the state of art in giving ECT and be able to present the treatment to the patient and the patient's relatives in a knowledgeable and scientific manner, in order to reduce the stigma and transmit the fact that it is no longer "shock" or "convulsive" treatment. Emphasis on the fact that it should not be the last resort treatment as stated in some treatment algorithms, but rather a first line therapy when indicated.

According to the World Psychiatric Association ethical guidelines known as the "Madrid Declaration", any psychiatrist who is not abreast of knowledge and with holds treatment from a patient is unethical (Okasha etal., 2000). That is to say withholding an effective treatment like ECT from a patient can be considered as unethical.

Based on the evidence derived from randomized controlled trials and extensive clinical experience for nearly 70 years, ECT is, presently, the most effective treatment for certain psychiatric disorders. In consideration of what can be achieved, the most transient memory disturbance is a moderate price. The benefit to risk ratio of ECT is usually favourable.

Principles of biomedical ethics, endorsed four principles of ethics. Without ranking their importance, the principles are

beneficence (doing good), nonmaleficence (not doing harm), autonomy (respect for the individual) and justice (being fair) (Beauchamp and Childress, 2001). Ottosson and Fink (2004) state that in most cases the use of ECT is in agreement with the principles of beneficence, nonmaleficence, and respect for autonomy. Sadly, the principle of justice is far from satisfied.

An urgent goal of mental health care should be to provide access to ECT and eliminate the severe impediments to its use, so long as it can defend evidence based superiority over other treatments.

Limitations of the study

The study was carried out in a selective group of patients who required admission in a private hospital which is not representative of the whole Egyptian patient sample; future studies should also include university and state hospitals. In depth study of prognosis of different patient diagnoses should be carried out in future studies as well as studies on ECT given on out patient basis.

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ممارسة العلاج بالجلسات الكهربائية في عينة من المرضى المصريين

Assessment of Neurochemical Alterations that Occur in Bipolar Patients Following Medication Using Proton Magnetic Resonance Spectroscopy.

Fikry M, Hussein M.

Abstract :

Several studies demonstrated the neurochmeical alterations in bipolar patients using proton magnetic resonance spectroscopy (MRS). Few studies compared between the changes that occur before treatment and that which occur after the patient achieved complete remission. Patients with bipolar disorder having manic episode were hypothesized to demonstrate metabolic abnormalities with in the anterior cingulate and that these abnormalities are altered with medication. Twenty patients with bipolar disorder (age 20-53 years, mean 29.5 ± 7.61) with a mean duration of (32.65 ± 12.93) to achieve complete remission were evaluated with proton MRS. The metabolic concentration of the anterior cingulate were calculated using a single voxel. The results of this study revealed that there is a significant decrease in the level of myo-inositol following treatment. In addition there is a trend towards increase in the level of N-acetyl aspartate following medication. However there was no significant difference in the level of choline and creatine. The results of this study suggest that there is abnormalities in the phosphoinositid cycle as evident by the significant changes that occur in the myo-inositol level. Changes that occur in N-acetyl aspartate level suggest that there is neuronal dysfunction in bipolar patients and that it may need more time to be more evident.

Introduction

Bipolar disorder is a common, life long illness that typically begins in late adolescence. The illness is implicated in functional impairment and represents an important risk factor for suicide ***(Oquendo and Mann, 2001***). However, the neurochemistry and pathogenesis of bipolar disorder remain poorly understood. Evidence implicating abnormal frontal circuitry in the pathophysiology of mood disorders is known ***(Soares and Mann, 1997).*** Morphometric measures of frontal (prefrontal and orbitofrontal) structures have demonstrated a trend for decreased volume particularly in gray matter ***(Lim et al, 1999; Sax et al, 1999)***. Cerebral blood flow and metabolism investigations suggest frontal hypometabolism in patients with mood disorders ***(Drevets et al. 1997)***. Consistent with these findings are histopathologic reports demonstrating marked reduction in density and size of cortical neurons and glial cells ***(Rajkowska, 1997; Ongur et al, 1998)***.

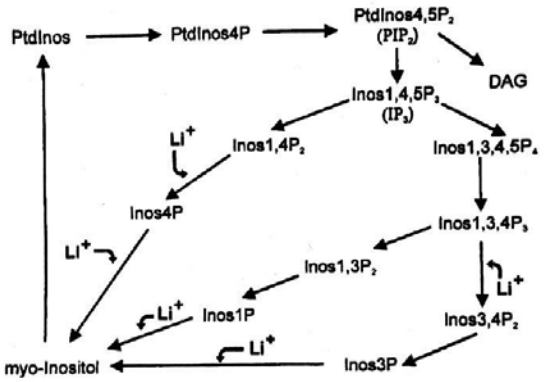
One strategy used to gain insight into the underlying pathophysiology of a disease/illness is to identify the mechanism(s) of action of medications which reduce symptom severity in the majority of patients afflicted with the disease/illness. There is mounting evidence suggesting that the phosphoinositide – protein kinase C (PI-PKC) signal transduction pathway is a common target of chronic mood stabilizer, atypical antipsychotic and antidepressant drugs ***(Calker and Belmarker, 2000)***.

Moreover, until very recently Lithium was the mainstay of long term treatment for

patients with bipolar disorder ***(Geddes et al, 2004)***. Lithium is an uncompetitive antagonist of inositol monophosphatase thus resulting in increased concentrations of the inositol monophosphates ***(Berridge and Irvine, 1989)***, and a corresponding decrease in myo-inositol concentration based upon these findings it was hypothesized that the clinical utility of lithium in bipolar disorder may be due to these actions on the PI cycle ***(Berridge et al, 1989)***.

Phosphotidylinositol (PI) is a major component of neuronal cell membranes. The phosphoinositide cycle (Fig 1) has been discovered as a major second messenger system ***(Berridge and Irvine, 1989)***. Receptor stimulation by neurotransmitters activates phospholipase C enzyme in a number of membrane receptor signaling pathways. Phospholipase C triggers the break-down of phosphatidylinositol-bis-phosphate (PIP2) to inositol 1,4,5 triphosphate (IP3), which releases calcium from internal stores. A series of phosphatases remove the phosphate groups from IP3 sequentially, releasing free inositol ***(Frey et al, 1998)***.

Figure 1 : Phosphoinositide cycle



Phospholipase C triggers the breakdown of phospahatidylinositol-bis-phosphate (PIP2) to inositol 1,4,5-triphosphate (IP3), which has a function as a second messanger. Lithium reduces brain levels of myo-inositol by inhibition of inositol-phosphatase. Frey et al 1998.

Magnetic resonance spectroscopy (MRS) is a non-invasive computerized imaging technique that relies on the same nuclear magnetic resonance (NMR) principles that form the basis of magnetic resonance imaging (MRI) and functional MRI (fMRI). It is used in both clinical and research settings to study brain chemistry, as it enables the relative quantification of certain compounds and their constituents in specific brain regions ***(Chakos et al, 1998)***. In psychiatry, MRS is increasingly used to research the neurochemical changes that occur in psychiatric disorders such as schizophrenia, dementia and affective disorders ***(Malhi et al, 2002)***. Recently it has been used to identify the neurochemical effects and predictors of response to medication commonly used to treat bipolar disorder ***(DelBello et al, 2006)***.

Over the past decade a growing number of magnetic resonance spectroscopic studies investigating the neurochemical basis of bipolar disorder have been accumulated. However, there have been mixed results from these studies preventing a conclusion

on the direction of the alterations expected on individual neurochemcials ***(Brambilla et al, 2005a)***.

With these considerations in mind, the aim of this study was to identify the neurochemical effects of treatment in bipolar patients presenting with manic with psychotic features in the anterior cingulate. We hypothesized elevated myo-inositol (MI) would reflect impaired phosphoinositide metabolism and decreased N acetyl aspartate (NAA), choline (Cho)and Creatine (Cr) of the prefrontal cortex would reflect impairments in neural function and that these metabolites are altered with medications.

Methodology :

Subjects:

Patients hospitalized with bipolar disorder receiving the diagnosis manic with psychotic features were recruited from consecutive admissions to the inpatient psychiatric units at the Institute of Psychiatry Ain Shams University Faculty of Medicine. Twenty patients were between 20 ad 53 years with a mean age (29.5 ± 7.61).

Twelve patients were male (60%) and 8 patients were female (40%). The diagnosis were made according to ICD10 using the ICD10 symptoms check list. The mean duration of the illness was 7.15 ± 5.33, with a mean age of onset 22.35 ± 6.6 and a mean number of episode 5.2 ± 3.49. Ten patients (50%) had a positive family history of mood disorder as out lined in table 1 and 2.

Patients with history of ICD10 substance dependence excluding tobacco, any major medical or neurological disorder, a history of head trauma, any contraindication to receiving a magnetic resonance imaging (MRI), a diagnosis of mental retardation were excluded from the study.

The institutional review boards of research of Ain Shams University Institute of Psychiatry approved the study protocol. All participants provided an informed consent after complete description of the study protocol was provided to them.

Procedures:

Manic symptoms were assessed using the Young Mania Rating Scale Score (YMRS) ***(Young et al, 1978)***. The mean score before starting any medication was 47.65 ± 6.1. The patient before scanning did not receive any medication except for Midazolam intravenous between 15 to 20 mg to sedate the patients during scanning as any slight movement affect the scanning. Medications to which the patient responded include mood stabilizer, antipsychotic and ECT are summarized in table 3. The medication was adjusted according to the protocol of each unit and patients' past history of medication to which they responded. The mean duration to which the patients achieved complete remission was 32.65 ± 12.93 to which the mean score of YMRS was 4.8 ± 2.04.

Magnetic resonance imaging and spectroscopy:

Structural imaging and spectroscopy were performed using a 1.5 T Philips Intera scanner and a quadrate proton head coil. Following sagital image localization, a 3D coronal volume scan (SPGR; 124/60 slices; matrix: 256 x 192; 1 NEX; Flip angle = 45; SLT = 1.5/3mm; TE = 5 ms; TR = 35 ms) was acquired for image segmentation and T2 weighted axial images were used for spectral localization.

Water suppressed localized spectra were acquired using a 16 x 16 MRS I grid [field of view : 16 x 16 cm; voxel size : 1 x 1 x 2 cm; in plan (axial) thickness : 2 cm] and the PRESS pulse sequence (echo time = 6000 ms; repetition time = 31 ms and 144 ms). A single voxel was centered on the anterior cingulate cortex and midline with sufficient tissue surrounding it being no closer than 1 cm from the skull.

Data were processed and pertinent metabolic ratios were obtained via intensity values generated by the machine. The spectral peak areas for Myo-inositol (MI), N-acetyl aspartate (NAA), choline (Cho) and creatine (Cr) were expressed as peak intensity curves in both short Fig (2,4) and long sequences (Fig 3,5).

Table (1): Descriptive analysis of the sample

	Minimum	Maximum	Mean ± Sd
Age	20	53	29.5 ± 7.61
Age of onset	16	43	22.35 ± 6.6
No. of episode	2	13	5.2 ± 3.49
Duration of illness	1	21	7.15 ±5.33
YMRS before treatment	30	54	47.65 ± 6.1
YMRS after treatment	2	8	4.8 ± 2.04
Time to B.L	15	55	32.65 ± 12.93

Table 2: Gender and Family history

Sex	Male	12	60%
	Female	8	40%
Family history	Positive	10	50%
	negative	10	50%

Patient	Age	Sex	Age of onset	No. of episode	Family history	Duration of illness	YMRS before treatment	YMRS after treatment	Time to return to baseline	Medications
1	30	M	17	12	Negative	13	52	6	55	Carbamazpine, Risperdone, ECT
2	23	F	21	2	Positive	2	50	7	35	Lithium, Haloperidol, ECT
3	30	M	25	5	Negative	5	52	4	34	Carbamazpine, Haloperidol, ECT
4	28	M	20	6	Positive	8	50	6	40	Lithium, Trifluperazine, ECT
5	25	M	20	5	Positive	5	54	8	28	Lithium, Olanzapine ECT
6	26	F	20	6	Negative	6	39	2	20	Carbamazpine, Haloperidol ECT
7	30	F	28	3	Negative	2	40	2	19	Lithium, Risperdone, ECT
8	20	M	16	4	Positive	4	49	8	53	Divaloprate. Clozapine ECT
9	28	F	16	12	Negative	12	50	4	25	Carbamazpine, Triflueperazine ECT
10	33	F	16	8	Positive	17	50	8	20	Lithium, Haloperidol, ECT
11	28	M	22	2	Negative	6	50	5	28	Lithium, Divaloprate, Aripiprazole ECT
12	26	F	16	4	Positive	10	43	5	20	Lithium, Risperdone, ECT
13	28	M	27	2	Positive	1	52	7	52	Lithium,Carbamazepine Risperdone, ECT
14	53	F	43	5	Negative	10	30	4	15	Carbamazpine,Chloropromazine
15	35	M	28	2	Negative	7	50	4	33	Lithium, Haloperidol, ECT
16	20	M	18	3	Negative	2	42	3	54	Lithium, Haloperidol, ECT
17	42	M	21	13	Negative	21	54	6	37	Lithium, Haloperidol, ECT
18	26	M	20	5	Positive	6	53	4	35	Lithium, Clozapine ECT
19	24	M	22	2	Positive	2	45	5	25	Lithium,Risperdone, ECT
20	35	F	31	3	Positive	4	48	2	20	Lithium, Haloperidol, ECT

Statistics: Statistical analysis was done using the Statistical Package for Social Sciences (SPSS) version 10. Wilcoxon Signed Ranks test was used to detect the difference between metabolites before and after medications

Results:

The result of our study reveal that there is significant decrease in myoinositol level (Z = 2.9, P<0.01), in the post medicated patients. However, although the increase in N-acetyl aspartate is non significant, there is a trend towards increase of NAA in most patients (Z=0.3, P>0.05). Moreover there is no statistical difference in Choline (Z=0.73, P>0.05). and creatine level (Z = 0.21, P>0.05). in patients following medication (table 4).

Figure 2: Premedication short

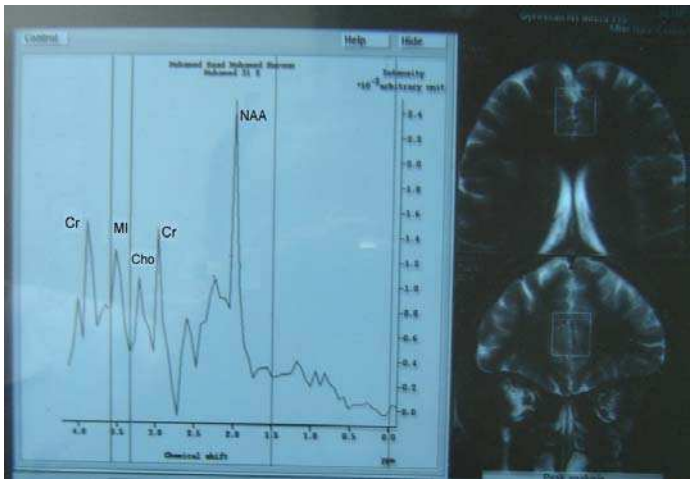


Figure (3): Pre-medication long

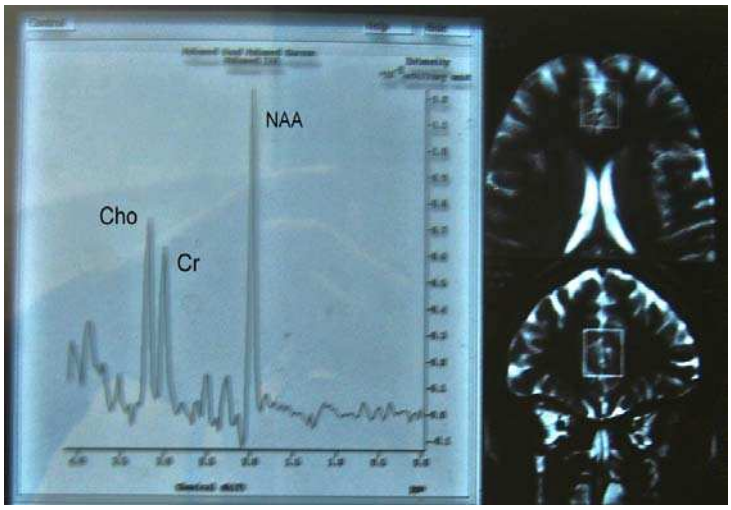


Figure 4: Post medication short

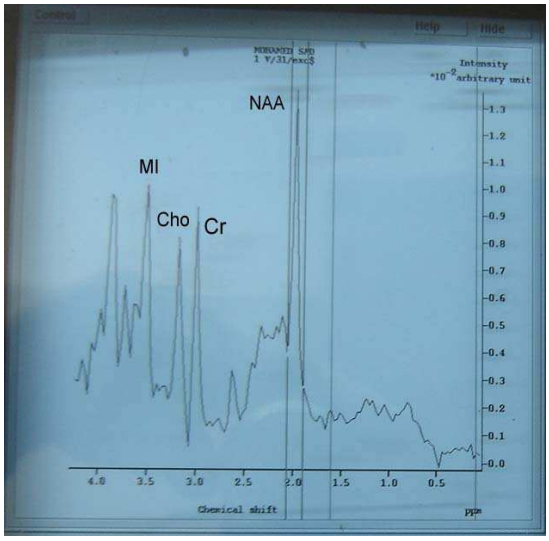


Figure 5: Post medication long

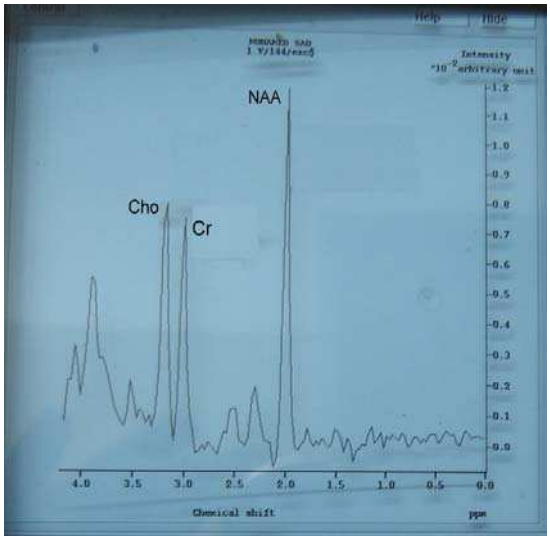


Table (4): Comparison between metabolites pre and post medication

	Pre medications			Post medications			Z value	Sign.
	Min	Max	Mean	Min	Max	Mean		
MI	53	515	162.6±125.9	36	150	75.7±29.6	2.9	<0.01
NAA	63	232	130±54.5	68	302	170±70.1	0.3	>0.05*
Cho	24	175	68.5±44.9	34	190	87.8±56.4	0.73	>0.05
Cr	8	224	99.4±56.1	20	176	98.5±48.9	0.21	>0.05

*although the p value of NAA is not significant, yet there is a trend towards increase.

Discussion:

Magnetic resonance spectroscopy (MRS) is a non-invasive approach that allows in vivo investigation of brain chemistry. The most commonly used spectroscopic approach is proton MRS (^{1} HMRS) which can detect myo-inositol (MI) N-acetyl aspartate (NAA), choline containing compounds (Cho) and creatine (Cr) which is composed of phosphocreatinine and creatinine which are high energy phosophate metabolites ***(Brambilla et al, 2004)***.

Anterior cingulate was chosen in this study since the prefrontal cortex has been linked to the regulation of the expression of emotional state. ***(Sax et al, 1999)***. Within the prefrontal cortex the anterior cingulate has extensive connections with other brain areas involved in emotional processing ***(Bush et al, 2002)***, such as amygdale, insula, thalamus and preiaqueductal gray matter, and orbital cortex ***(Lane et al, 1998; Barbas, 2000)***. Therefore it has been implicated in the pathophysiology of

bipolar disorder because it participates in modulating decision making, planning and mood regulation ***(Drevets et al, 1998, Vogt et al, 2003)***.

Myo-inositol (MI):

Myo-inositol plays a crucial role in the transduction of signals in the brain acting as a second messenger and being the key intermediate of the phosphinositol pathway and the substrate for recycling of inositol phospholipid ***(Stanley, 2002)***

The results of our study indicate that there is significant reduction of the myo-inoistol level following complete remission. This is in agreement with previous reports ***Davanzo and colleagues 2001***, who found increased myo-inositol level in the anterior cingulate cortex of children with bipolar disorder during the manic phase and subsequent decease following 7 days of lithium intake. Also ***Cecil et al, 2003***, reported 16% elevation in the myo-inositol concentration in the frontal cortex in bipolar patients in the manic phase. Moreover other studies investigating the euthymic state found no difference in the level myo-inositol between patient and healthy control ***(Winsberg et al, 2000; Silverstone et al 2002; chang et al, 2003)***. The results of our study support the hypothesis of previous studies that in bipolar patients who are acutely ill, there is abnormal PI cycle activity. In euthymic patients any abnormalities in PI cycle functioning are normalized possibly secondary to the effect of medications.

N-acetyl aspartate (NAA) :

N-acetyl aspartate is the second abundant aminoacid after glutamate, in the human brain and is the most prominent peak in the proton spectrum after water. NAA is found only in the mature neurons and is thought to be a marker of neuronal integrity, viability and activity ***(Urenjak et al, 1993)***. Our results reported a trend towards an increase in NAA concentration following medications. This is in agreement with ***Moore et al 2000*** who reported an increase in NAA concentration with in the frontal lobe following 4 weeks of lithium therapy in adult patient. Consistent with these finding ***DelBello et al 2006*** who reported olanzapine remitters patients exhibited a greater increase in medial ventral prefrontal NAA level compared with non-remitter. Also **Cecil et al 2003** reported 8% lower for NAA level in children with a mood disorder with in the cerebellar vermis compared with healthy children. Furthermore increased bilateral thalamic NAA levels have been shown in euthymic male patients with bipolar 1 disorder compared with healthy control ***(Deicken et al, 2001)***. ***Brambilla et al 2005a*** concluded that this increase in NAA level may reflect neuronal hypertrophy, reduced glial density or abnormal synaptic or dendritic pruning. The result of our study though revealed only a trend towards increase in NAA level yet it is preliminary and needs replication with assessment of the effect of medication on the long term basis and its effect on the structure changes that occur due to medications.

Choline (Cho):

Choline (Cho) resonance is predominantly composed of phosphorylcholine (PC) and glycerophosphoryl choline. Therefore, the Cho Peak is considered as a potential biomarker for the status of membrane phospholipids metabolism ***(Moore and Galleway 2002)***. The results of our study find no significant difference between choline level before and after medication. This is consistent with other studies where

subjects were mostly on lithium which couldnot detect any significant difference in choline levels between patients and controls in different brain regions ***(Stoll et al, 1992; Bruhn et al, 1993; Kato et al, 1994; ohara et al, 1998; Amaral et al, 2002; Brambilla, 2005b)***. However other studies reported increased choline in the basal ganglia of euthymic bipolar patients compared with healthy subjects, a findings not attributable to lithium since most of the subjects on these studies were not taking lithium ***(Sharma et al, 1992; Lafer et al, 1994; Kato et al, 1996; Hamakawa et al, 1998)***. Another study by ***Moore et al 2000*** reported increase choline in the right cingulate cortex compared with control subjects. From the previous studies ***Bramella et al 2005a*** concluded that elevated choline levels in bipolar disorder if present may be specific for basal ganglia and may be independent of lithium treatment suggesting alterations in membrane metabolism.

Creatine (Cr)

Creatine peak reflects the presence of both creatine and phosphocreatine. The equilibrium between creatine and phosphocreatine is determined by the cellular demand for high energy phosphate stored as creatine phosphate ***(Moore and Galloway, 2002)***. The results of our study revealed that there is no statistical difference between creatine level before and after medication. This is consistent with other studies which investigated the level of creatine during the manic phase in the dorsolateral prefrontal cortex, medial orbital cortex and prefrontal cortex and find no significant difference between patients and control ***(Cecil et al, 2002; Micheal et al, 2003)***. Other studies as ***Hamakawa et al 1998, 1999 and Brambella et al 2005b*** also reported no significant difference between euthymic bipolar patients and normal cortrol in the basal ganglia, frontal cortex and dorsolateral prefrontal cortex. Moreover studies investigated the depressive phase ***Friedman et al 2004 and Dager et al 2004*** reported the same result in cingulate, thalamus, parietal and occipital lobe. Therefore it seems that the level of creatine is relatively constant through out the phases of the illness.

Limitation of the study:

It should be pointed out that the present study has a number of limitations. We only investigated metabolism in the anterior cingulate cortex using a single voxel technique with inability to compare between the right and left cingulate as this would need more time with equivalent increase in sedation doses. Also the small number of the subjects with heterogeneity regarding the duration of the illness, family history and medication used.

In conclusion we have noted alterations in the myo-inositol level and N-acetyl aspartate in the anterior cingulate before and after treatment. However, the results of this study is very preliminary and need further replication taking in consideration larger samples, other phases of the illness as depressive and mixed phases, first episode patients with longitudinal studies, using same treatment and further detailed analysis of the aminoacid moieties

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Bipolar Mood Disorder Among Children of Attention Deficit Hyperactivity Disorder

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Abstract

Bipolar mood disorder is one of the most difficult disorders to recognize in children because it does not fit precisely the adult criteria. Since there is overlap regarding major symptoms between Bipolar Mood disorder and Attention Deficit Hyperactivity disorder in children, we hypotheses that Attention Deficit Hyperactivity disorder is over diagnosed and Bipolar Mood disorder is under diagnosed. One hundred and twenty children have the diagnosis of Attention Deficit Hyperactivity disorder were reevaluated for Bipolar Mood disorder using DSM-IV-TR., Conner's Rating Scale, Achenbach's Child Behavior Checklist, Clinical Administered Rating Scale for Mania and Parent Version of the Young Mania Rating Scale. Out of 120 Attention Deficit Hyperactivity disorder Children, 45 children (37.5%) were re-diagnosed and met the criteria of Bipolar Mood disorder. There were statistical significant difference between the two groups regarding gender, type of school, family history of Bipolar Mood disorder and social and sport participation. We concluded that Bipolar Mood disorder can be misdiagnosed in children as Attention Deficit Hyperactivity disorder so these children will not receive their proper management and be socially impaired with high level of behavioral difficulties, school failure and poor academic performance.

Introduction

Although bipolar mood disorder (BPD), is probably the most prevalent psychotic disorder in adults, it has been relatively neglected in children and adolescents over the past century (Anthony and Scott, 2000). The literatures on early onset BPD that estimated prevalence, particularly before puberty, is limited by historical biases against pediatric mood disorders and by formidable diagnostic complexity and co morbidity (Weinberg and Brumback, 1976). Although clinical features of pediatric and adult BPD have similarities, pediatric cases probably cannot be defined solely by features characteristic of adult cases. Onset was before age 20 years in at least 25% of reported BPD cases, with some increase in this incidence over the past century (Carlson, 1999). Pediatric BPD episodes frequently include irritability, dysphoria, or psychotic symptoms; they are commonly chronic and carry high risks of substance abuse and suicide. BPD is often recognized in adolescents, but the syndrome or its antecedents are almost certainly under recognized and under treated in children (Weller, *et al.,* 2001; Adler, *et al.,* 2005; Faraone, *et al.,* 2005; Kowatch, *et al.,* 2005; Udal and Groholt, 2006). Controlled studies of short and long term treatment, course, and outcome regarding BPD remain strikingly limited, and the syndrome urgently requires increased clinical and scientific interest. The relationship between BPD and attention-deficit hyperactivity disorder (ADHD) in children has been one of the most hotly debated topics in recent child psychiatry (Giedd, 2003). At the heart of matter, there is a large numbers of children with bipolar disorder are being unrecognized or misdiagnosed (Pliszka, 2001). It was reported that the most

diagnostic clinical dilemmas seem to arise in child psychiatry from overlapping symptomatology between BPD and ADHD (Sachs, *et al.,* 2003). Prominent hyperactivity and impaired concentration in ADHD make a problem in differential diagnosis with early BPD, and the two are strongly related. Since these disorders share features, misdiagnosis may occur, probably more often in children than in adolescents (Biederman, *et al.,* 2002). A recent study helps to clarify this relationship: 91% of children evaluated with current or previous mania also met criteria for ADHD, while only 19% with a diagnosis of ADHD also met DSM-VI-TR criteria for current or previous mania. Similar diagnostic criteria persisted even after elimination of obviously similar symptoms found in both disorders, such as hyperactivity, talkativeness, and distractibility (Wozniak, *et al.,* 2003; Adler, *et al.,* 2005; Faraone, *et al.,* 2005; Kowatch, *et al.,* 2005; Udal and Groholt, 2006). Hyperactivity, impulsivity, and inattention are seen in children with ADHD and BPD, but these two disorders are radically different in terms of the impact that they have on a child's life. Determining causes of child behavioral problems is extremely important. ADHD is far less severe regarding impairment than BPD. The most important problems for an ADHD child are how to slow down, focus, and organize his life. The most important problem for a child with BPD is how to manage his mood shift from potentially destructive hypomania, to a depression, so dark that it can be paralyzing or suicidal (Akiskal, 2000). It may be difficult to distinguish bipolar disorder from ADHD. Ninety eight percent of children with the diagnosis of BPD also qualify for the diagnosis of ADHD because of the presence of inattention, impulsivity, and hyperactivity which are seen in the ADHD patients (Wozniak, *et al.,* 2003). Conversely, twenty two percent of those children diagnosed with ADHD fit the criteria for BPD (Butler, *et al.,* 2000). It is extremely important to identify children with dual diagnosis (BPD and ADHD) in order to receive proper management and get better quality of life. We have to test the hypothesis that ADHD may be a childhood version of BPD among some children and to study the impact of BPD among children on their social competencies, behavioral, and academic performance.

Subjects and Methods

Subjects:

A cross sectional comparative study was carried out over one year period on children attending the Neuropsychiatry Outpatient Clinic in Suez Canal University Hospital. One hundred and twenty children coming for follow up of their ADHD, diagnosed according to DSM-IV-TR criteria without co morbid psychiatric disorder, were included in our study. Our group study had fulfill the following including criteria**:** children aged 6-12 years old, the child must be accompanied by at least one of his or her parents and consent was obtained from one of the parents. Children with epilepsy, other apparent neurological manifestations or any sign or symptom suggestive of physical disorder were excluded from the study.

Sampling strategy:

Woolston and Mayes (2001) study the rates of bipolar disorder in a group of ADHD in child Neuropsychiatry Outpatient they found that 23%children how diagnosed as ADHD were re-diagnosed and met the criteria for BPD. Z X p (1- p)

The sample size was 120 children according to the following equation: N = -D2

Methods:

Children in our study were examined and subjected to: fully detailed psychiatric sheet designed in our psychiatry department, using DSM-IV-TR diagnostic criteria. The interview with one or both parents, the evaluation included observation of the child behavior, the child parent interaction and the separation process. Parents were asked to fill the questionnaires independently. Those who can not read were helped by the interviewers.

Methodological Tools :

I- Conner's Rating Scale

It is one of the most widely used scales in rating behavior. A total score is derived from the scale and the cut off score of 15 has been established as the point that confirms the presence of ADHD since it is very much above the scores received by normal children (Conner, 1969). Conner's scale appears to distinguish with good and accepted precision between normal and hyperactive disturbed children. In order to facilitate the practical use of this scale it was translated to Arabic language and was given to referees to comment on the adequacy and fluidity of the items compared to the original version (El-Defrawi, *et al.,* 1992). In Egypt, Conner's ADHD scale, when applied to children diagnosed as having ADHD, appeared to be very effectively differentiating them from children with no psychiatric complaints. However, the score of 15 is low especially for young children (6-8 years) and in spite of statistical distinction between normal children and children referred for ADHD, it may lead to identification of false positive for this reason**,** EI Defrawi, et al., (1992) have suggesting raising the cut off score for behavioral problems up to 19 points.

II- Achenbach's Child Behavior Checklist (CBCL) (1982)

The Child Behavior Checklist (CBCL) was developed by Achenbach, (1979) and modified by Achenbach and Edel-brock, (1983). It was designed to provide mental health professionals with a reliable means of assessing the behavior problems and social competencies of children referred for treatment. More recently direct observation Achenbach, (1988), revised the method of scoring of the parent CBCL and extended the range of scores on each behavior problem scales. In epidemiological studies it is used as a screening instrument for case identification (Bird, *et al.,* 1987). Another version was done by Achenbach and Edel-brock, (1991), it is one of the most extensively used parent report questionnaires that assess social competencies and behavioral problems among children aged 4 to18 years old (Achenbach and Edel-brock, 1983; 1991)**.** The CBCL is designed to obtain standardized parents report of children's problems and competency**.** It is for ages 4 to 18 and can be completed in 15 to 17 minutes. Rigorous cross-cultural comparisons of CBCL data have been reported on children from USA, Holland, Thailand, Australia and French (Achenbach and Edel-brock, 1987; Verhulst, *et al.,* 1995; Offord, 1995). According to Achenbach and Edel-brock, (1991), maternal reports were compared with initial teacher reports and the means of both were used to contrast differences between boys and girls. The CBCL is designed to be self-administered by parents who have at least fifth grade reading skills, but it can also be administered by an interviewer. Arabic

version of CBCL was done by El Defrawi, *et al.,* (1991), the instrument was initially translated into Arabic for use with Egyptian parents; the translation was reviewed by child psychiatrists and clinical psychologists who are fully bilingual. After being modified in the course of this review, the instrument was back translated by a professional translator from the university, the bilingual mental health professionals reviewed the back translation to ensure that the connotations of the original CBCL items were accurately captured and vernacular expressions were added where necessary to facilitate understanding. Achenbach's child behavior checklist, contains 113 items for which a parent and/ or teacher uses a three-point scale to rate each behavior. According to the parent report:

A) Internalizing factors are anxious, schizoid, depressed, uncommunicative, obsessive compulsive, somatic complaint and social withdrawal. **B) Externalizing factors** are hyperactive, aggressive and delinquent. Since the norms for the CBCL are based on no clinical (normal) samples, the CBCL may be used to determine whether a child exhibits unusual or excessive behaviors relative to normal children.

III- Clinician-Administered Rating Scale for Mania (CARS-M):

The CARS-M is a 15-item clinician-administered scale designed to assess the severity of both manic and psychotic symptomatology in children. Most items are scored from 0 (absent) to 5 (symptom present to severe degree), based on increasing severity. One item is scored from 0 to 4. The CARS-M takes approximately 15-30 minutes to administer (Pavuluri, 2002). The CARS-M may be used to assess the severity of a manic state for either clinical or research purposes. Because it is compatible with DSM-IV criteria, it may be used to evaluate the presence of manic symptoms in order to facilitate diagnostic assessment. Psychotic symptoms also may be assessed with the CARS-M. For studies investigating patient responses to clinical treatment, the CARS-M can provide a reliable measure of efficacy. This rating scale help parents and teachers recognize mania in children and adolescents (Alessia, *et al.,* 2002). The CARS-M contains 2 subscales, each of which is scored separately. To derive the mania subscale score, items 1 through 10 are summed. To gauge severity level, the following cut off points is recommended: 0-7 none or questionable mania; 8-15 mild; 16-25 moderate; and 26 or greater indicates severe symptomatology. The second subscale, which measures psychotic symptoms/ disorganization, is derived by summing items 11 through 15. Both subscale scores may be totaled to yield a global measure of mania with psychotic features. However, the total score should not be used to measure severity of mania, but rather, only subscale 1 scores (items 1 to 10). The two subscales allow for the independent assessment of manic versus psychotic symptoms, which may respond differently to treatment (Campbell, *et al.,* 2002). It was translated by the researchers and was revised by three experts in the filed to take their consent to use it as a clinical tool.

IV- Parent Version of the Young Mania Rating Scale (P-YMRS)

The P-YMRS consists of eleven questions that parents are asked about their child's present state. The original rating scale (Young Mania Rating Scale) was developed to assess severity of symptoms in adults

hospitalized for mania (Young, *et al.,* 1978). It has been revised in an effort to help clinicians such as pediatricians determine when children should be referred for further evaluation by a mental health professional (such as a child psychiatrist), and also to help assess whether a child's symptoms are responding to treatment (Poolsup, *et al.,* 1999). The scale is intended to diagnose BPD in children. This version has been tested in a pediatric research clinic with a high number of children with bipolar disorder (Barbar, *et al.,* 2002). The child's total score is determined by adding up the highest number circled on each question. Scores may range from 0-60. Extremely high scores on the P-YMRS increase the risk of having BPD by a factor of 9, roughly the same increase as having a biological parent with bipolar disorder. Low scores decrease the odds by a factor of ten. Scores in the middle don't change the odds much (Barbar, *et al.,* 2002). The average scores in children studied were approximately 25 for mania (a syndrome found in patients with BPDI), and 20 for hypomania (a syndrome found in patients with BPD2, BPD-NOS, and Cyclothymia). Anything above 13 indicated a potential case of mania or hypomania for the group that was studied, while anything above 21 was a probable case. In situations where the odds of BPD diagnosis are high to begin with (e.g., a child with mood symptoms with 2 parents having bipolar disorder), the P-YMRS can be extremely helpful. But for most groups of people, the base rate of BPD is unknown but low. Then, the most that a high score can do is raising a red flag (similar to having a family history of BPD) (Kaufman, *et al.,* 2001). It was translated by the researchers and was revised by three experts in the filed to take their consent to use it as a clinical tool.

Statistical Analysis:

Descriptive statistics such as number of patients, percentages and means were used to describe the study population. For Comparative statistics, we used student t-test to compare means and chi square test to compare percentages. Data were collected, entered into personal computer and analyzed using EPI-Info version 6.04 software (CDC, 2001) and SPSS V.13 software (SPSS, 2002). Statistical significance was set at 5% level ($p \leq 0.05$).

Results:

Out of 120 Attention Deficit Hyperactivity disorder Children, 45 children (37.5%) were re-diagnosed and met the criteria of Bipolar Mood disorder (Table, 1). There were statistical significant difference between BPD group and ADHD group regarding gender, type of school, family history of BPD but no significant difference regarding age, residence and socioeconomic status (Tables, 2; 3). BPD group has statistically significant higher scores (Mean= 36.89±10.59) than ADHD group (Mean= 9.17±2.00), regarding YMRS-Parent Version as shown in table (4). BPD group has statistically significant higher scores (moderate to severe degrees) than ADHD group (normal to mild degrees), regarding CARS-M as reported by parent (Table, 5). ADHD group has statistically significant higher scores (mean= 27.76±12.00) than BPD group (mean= 18.78±4.59), regarding Conner's Rating Scale parent form (Table, 6). BPD group has statistically significant higher scores than ADHD group in sport participation (Table, 7), but not in joining sport club (Tables, 8), according to CBCL. There were statistical significant difference between BPD group and ADHD group regarding social and hobbies, academic performance

and externalizing or internalizing problems (Tables, 9-14). Finally, we put predictors of BPD in children as family history of BPD, disturbances in relationship with parents and siblings, good number of friends, frequent involvement in social activities, participation in house chores, arithmetic skills, school failure, YMRS-Parent Version score, CARS-M score and Conner's score (Table, 15).

Table (1): Re-diagnosis of ADHD children as BPD.

Children with BPD		Children with ADHD		Total
No	%	No	%	
45	37.5	75	62.5	120

Table (2): Demographic Variables of Both BPD and ADHD Groups.

Demographic Variables	BPD Group N=45		ADHD Group N=75		P Value
	N	%	N	%	
Age (Years) 6-8	13	28.9	23	30.7	0.321
8-10	19	42.2	39	52	
10-12	13	28.9	13	17.3	
Sex Males	26	57.8	49	65.3	
Females	19	42.2	26	34.7	0.040*
Residence Urban	33	73.3	45	60	0.134
Rural	12	26.7	30	40	
School Type Private	12	26.7	9	12	0.048*
Government	32	71.1	61	81.3	
No school	1	2.2	5	6.7	
Socioeconomic Low	15	33.3	33	44	0.246
Middle\High	30	66.7	42	56	

*Statistically significant

Table (3) BPD group and ADHD group on Family history.

Family History	BPD group N=45		ADHD group N=75		P Value
	N	%	N	%	
BPD	23	51.1	7	9.3	0.001*
ADHA	0	0	3	4	
Other psychiatric disorder	3	6.7	5	6.7	
No family history psychiatric disorder	19	42.2	60	79	

*Statistically significant

Table (4): BPD group and ADHD group according to Young (YMRS-Parent Version).

Psychiatric diagnosis	Number	Mean	S.D	P value
BPD	45	36.89	10.59	0.001*
ADHD	75	9.17	2.00	

*Statistically significant

Table (5): BPD group and ADHD group according to (CARS-M) as reported by parents.

CARS-M	BPD group N=45		ADHD group N=75		P value
	N	%	N	%	
Non	0	0	52	69.3	0.001*
Mild	6	13.3	23	30.7	
Moderate	33	73.3	0	0	
Sever	6	13.3	0	0	

*Statistically significant

Table (6): BPD group and ADHD group according to Conner's Rating Scale parent form.

Psychiatric diagnosis	Number	Mean	S.D	P value
BPD	45	18.78	4.59	0.001*
ADHD	75	27.76	12.00	

*Statistically significant

Table (7): BPD group and ADHD group on Sport Practice according to the CBCL.

Sport Practice	BPD group N=45		ADHD group N=75		P Value
	N	%	N	%	
Actual sport practice	N= 45		N=75		
Participating	**17**	**37.8**	**17**	**22.7**	
Not participating	**28**	**62.2**	**58**	**77.3**	**0.044***
Time spent in sport activity	N=17		N=17		
Don't know	**0**	**0**	**4**	**5.3**	
Less than average	**4**	**8.9**	**11**	**14.7**	
Average	**11**	**24.4**	**2**	**2.7**	**0.001***
More than average	**2**	**4.4**	**0**	**0**	
Degree of skillfulness in sport activity	N=17		N=17		**0.001***
Don't Know	**0**	**0**	**4**	**5.3**	
Less than average	**11**	**24.4**	**13**	**17.3**	
Average	**6**	**13.3**	**0**	**0**	
More than average	**0**	**0**	**0**	**0**	

*Statistically significant

Table (8): BPD group and ADHD group in joining sport club according to CBCL.

Joining club	BPD group N=45		ADHD group N=75		P Value
	N	%	N	%	
Joining	**9**	**20**	**14**	**18.7**	**0.858**
Not joining	**36**	**80**	**61**	**97**	

Table (9): BPD group and ADHD group in Hobbies according to CBCL.

Hobbies	BPD group N=45		ADHD group N=75		P Value
	N	%	N	%	
Yes	**19**	**42.2**	**19**	**25.3**	
No	**26**	**57.8**	**56**	**74.7**	**0.045***

*Statistically significant

Table (10): BPD group and ADHD group participation in house chores according to CBCL.

Participation in house chores	BPD group (N=45)		ADHD group (N=75)		P Value
	N	%	N	%	
Participating	**30**	**66.7**	**25**	**33.3**	
Don't participating	**15**	**33.3**	**50**	**66.7**	**0.001***

*Statistically significant

Table (11): Social Competence between BPD group and ADHD group according to CBCL.

Social competence	BPD group (N=45)		ADHD group (N=75)		P Value
	N	%	N	%	
Relation with parents					
Worse	**20**	**44.4**	**45**	**60**	
About the same	**20**	**44.4**	**20**	**26.7**	**0.001***
Better	**5**	**11.2**	**10**	**13.3**	
Relation with siblings					
Worse	**16**	**35.6**	**38**	**50.7**	
About the same	**19**	**42.2**	**33**	**44.0**	
Better	**10**	**2.2**	**4**	**5.3**	**0.001***

*Statistically significant

Table (12): Social activities in BPD group and ADHD group according to CBCL.

Social activity	BPD group (N=45)		ADHD group (N=75)		P Value
	N	%	N	%	
Number of friends					
No friend	**0**	**0**	**24**	**32**	
One friend	**5**	**11.1**	**39**	**52**	**0.001***
Two or three friends	**11**	**24.4**	**11**	**14.7**	
Four friends or more	**29**	**64.5**	**1**	1.3	
Social involvement with friends					**0.001***
Less than one time	**2**	**4.4**	**58**	**77.3**	
One or two times	**6**	**13.4**	**16**	**21.4**	
Three or more times	**37**	**82.2**	**1**	**1.3**	

*Statistically significant

Table (13): BPD group and ADHD group in school performance according to CBCL.

School performance	BPD group (N=44)		ADHD group (N=70)		P Value
	N	%	N	%	
School failure	**24**	**54.5**	**41**	**58.6**	
No School failure	**20**	**45.5**	**29**	**41.4**	**0.535**

N.B: 6 children were drops out from school (one child from the BPD group and 5 children from the ADHD group).

Table (14): BPD group and ADHD group on academic performance according to CBCL.

Academic subjects	BPD group (N=44)		ADHD group (N=70)		P Value
	N	%	N	%	
Performance in Arabic subject					
Failure	**8**	**18.2**	**37**	**52.9**	**0.001***
Less than average	**12**	**27.2**	**27**	**38.6**	
Average	**16**	**36.4**	**6**	**8.5**	
More than average	**8**	**18.2**	**0**	**0**	
Performance in Arabic spelling					
Failure	**7**	**16**	**42**	**60**	**0.001***
Less than average	**18**	**41**	**28**	**40**	
Average	**11**	**25**	**0**	**0**	
More than average	**8**	**18**	**0**	**0**	
Performance in Arabic reading					
Failure	**8**	**18**	**42**	**60**	**0.001***
Less than average	**20**	**45.5**	**28**	**40**	
Average	**7**	**16**	**0**	**0**	
More than average	**9**	**20.5**	**0**	**0**	
Difficulty in arithmetic					
Failure	**34**	**77.3**	**45**	**64.3**	**0.877**
Less than average	**9**	**20.5**	**19**	**27.2**	
Average	**1**	**2.2**	**6**	**8.5**	
More than average	**0**	**0**	**0**	**0**	

*Statistically significant

N.B: 6 children were drops out from school (one child from the BPD group and 5 children from the ADHD group).

Table (15): Multiple regression analysis for the predictors of BPD in children.

Parameters	Odds ratio	95% Confidence Interval		P value
		Lower	Upper	
1. Age	0.98	0.14	1.12	0.322
2. Sex	0.69	0.26	0.95	0.408
3. Residence	2.20	0.31	2.51	0.138
4. School	0.31	0.26	0.57	0.575
5. Family history	40.60	0.66	41.26	< 0.0001**
6. Sport particiption	3.43	0.34	3.77	0.064
7. Joining club	0.03	0.16	0.19	0.857
8. Hobbies	3.71	0.35	4.06	0.054
9. House chores	9.35	0.19	13.10	< 0.001**
10. Relation with siblings	33.70	0.65	34.35	< 0.001**
11. Relation with parents	38.47	0.61	39.08	< 0.001**
12. Number of friend	69.04	1.42	70.46	< 0.001**
13. Social activity	84.93	1.35	86.28	< 0.001**
14. School faliure	13.75	0.21	13.96	< 0.001**
15. Airthmetc skill	33.69	0.68	34.37	< 0.001**
16. Conners scale	19.94	5.34	25.28	< 0.001**
17. Cbcl scale	10.2	2.26	2.10	0.075
18. Cars for mania	100.95	11.70	112.65	< 0.001**
19. Ymr scale- parent version	96.59	24.50	121.09	< 0.001**

** Statistical significant at the 0.01 levels.

Discussion

The present study was designed to test the hypothesis that ADHD is a childhood version of BPD in some children and to study the impact of BPD in children on their social competencies, behavioral, and academic performance. It was found that 45 (37.5%) children out of 120 children diagnosed as ADHD were re-diagnosed and met the criteria for BPD**.** Our result was supported by other studies that found similar rates of BPD in hospitalized children with ADHD (Butler, *et al.,* 2000; Faraone, *et al*., 2000; Geller, *et al.,* 2002). Testable hypotheses might explain the high rates of incorrect diagnosis of ADHD Co morbidity is a chance phenomenon and symptoms of ADHD that precede the onset of BPD represent a pre-pubertal expression of illness antecedent to the development of a full mood episode, that ADHD may be an "age specific manifestation of BPD. The predictive significance of early ADHD symptoms for the ultimate development of BPD is debatable. Some investigators have proposed that ADHD may represent an age-specific manifestation of BPD, while others argue that the two disorders are separate and co morbid, with perhaps one (ADHD) increasing the risk of development of the other (BPD) (Biederman, 1999). Other possibility—that children with ADHD who go on to manifest mania-like symptoms

have "bad" ADHD or a new diagnostic entity altogether—has also been proposed (Jensen, 2005).

Demographic variables of both bipolar and ADHD groups: There was no significant difference between children with BPD and those with ADHD as regard to age. But the distributions of psychiatric disordered children were present more at age 8-10 years, which was found to be consistent with other previous studies (Khashaba, *et al.,* 1997; Szatamri, *et al.,* 1997; El-Batrawy, *et al.,* 2004). Our result could be explained on the assumption that in our culture there is a strong tendency to delay referral of the child to clinics and hope that child will grow out of it. Moreover our culture is more tolerable to children with disturbed behavior than many other cultures. In contrast to our finding some researchers in well designed prospective studies gave the light that bipolar disorder showed three peaks of onset; first from 15 to 19 years, followed by the age range from 20 to 24 years and another peak is the age above 65 years, with a mean age of onset of 18 years (Goodwin and Jamison, 1990; Keck, *et al.,* 2001). The cause of this stratified nature of age of onset is still under work but many hypotheses had been given as over secretion of cortisol, super fast biologic clock located in the suprachiasmatic nucleus or excessive influx of calcium into brain cells which assumed to be preprogrammed (Simon, 2003).

As regard to sex: there was significant difference between children with BPD and those with ADHD disorder which was consistent with the results of previous studies (El-Defrawi, *et al.,* 1995; Szatmari, *et al.,* 1996; Simon, 2003). Reasons for this gender discrepancy remain obscure; however, it could be explained by the assumption that the disorder is genetically determined with polygenetic inheritance. It is assumed that the females have a higher threshold of phenotypic expression than males (Mubarak and Shamah, 1999). Our result was inconsistent with previous reports that BPD was equally distributed in between both sexes (Keck, *et al.,* 2001).

As regard to residence, there was no significant difference between BPD group and ADHD group as regards residence, this result may be due to the nature of Ismailia area which content rural, semi rural and urban and there is no big difference between different areas. Our results are inconsistent with Okasha, 1988 and El-Akabawy, *et al.,* 1982, who pointed that psychiatric symptoms and disorders are more common in rural Egypt than urban Egypt.

As regard to the type of school: there was significant difference between children with BPD and children with ADHD according to the type of school, but we found the distribution of children with BPD according to the type of school was in private school 12 (26.7%) and government 32 (71.1%), compared to 9 (12%) and 61 (81.3%) respectively in ADHD children. This result can be explained by the low to moderate socioeconomic resources of Ismailia area. In consistent to this result, Farrag *et a*l., (2002), study the relationship between BPD and ADHD and type of the school in Assiut, they found that pupils in national schools had significantly more psychiatric disorders (BPD and ADHD) than those in private school. These results could be related to the selection criteria for admission in private schools, students usually come from higher social classes. In-addition, most private schools had environmental advantages, less

overcrowded classrooms and relatively high quality teachers.

Regarding the family history: We found that positive family history of BPD was reported in 51.9% in BPD children compared to 9.31% in ADHD children. This finding is similar to previous studies that reported that biological especially genetic factors are one of the most important risk factors of BPD in children. Some of this studies tried to find a relation between BPD and specific genetic loci, where certain loci of different chromosomes where found to have a link with BPD as chromosomes X, 5, 11, 12, 13 and 18 (Pollock, *et al.,* 2003; Simon, 2003). In this study there is no significant difference between children with BPD and those with ADHD regarding the family history of ADHA, we found the that there is no children with BPD had a family history of ADHD, and those with ADHD had a family history of ADHD 3 (4%). This finding is consistent with the results of El-Batrawy, *et.al.* (2004), who found no significant difference between children with BPD and those with ADHD regarding the presence of family history of hyperactivity or misconduct behavior. But our result was inconsistent with results of other studies where the authors found that early onset type of BPD was commonly preceded by a family history of ADHD (Sachs, *et al.,* 2000; Spencer, *et al.,* 2002; Weckerly, 2002). This contradiction could be explained by cultural and educational level of parents in our sample and the degree of their orientation to their children symptoms, which may give us a false negative or may be bias in our sample.

Regarding results of Young Mania Rating Scale Parent Version: It is often clinically difficult to differentiate BPD from other mental health conditions in children especially ADHD (Fristad, *et al.,* 1999; Bowring and Kovacs, 2002; Weller, *et al.,* 2003). Our result showed that there was significant difference between BPD children and ADHD groups regarding to Young Mania Rating Scale Parent Version (YMRS- Parent Version) that was in agreement with Fristad, *et al.*, (2002), who found that YMRS- Parent Version scores were significantly higher in manic versus ADHD children. Also, YMRS is not only useful in differentiating mania from ADHD but also in determining the severity of mania in pre-pubertal children (Poolsup, *et al.,* 2001; Weller, *et al.,* 2003).

Regarding results of Clinical Administered Rating Scale for Mania: It was found that there was significant difference between BPD group and ADHD group in Clinical Administered Rating Scale for Mania (CARS-M) as reported by parents as expected**.** Geller, *et al*., (2001), found that the (CARS-M) detected 88% of the children with BPD. Alicia, *et.al*. (2004), reported that Clinical Administered Rating Scale (CARS-M) was more specific to some manic presentations. Our study provided additional evidence of the validity of the (CARS-M) for screening children for BPD. So, our study provided additional evidence of the validity of the (CARS-M) for screening children for BPD.

Regarding results of Conners' Rating Scale: There was significant difference between BPD children and ADHD group regarding Conners' Rating Scale which was consistent with the results of El-Batrawy, *et al.*, (2004), but inconsistent with the results of Fristad, *et al.*, (2001) and Thomas, *et al*., (2004), who found that scores on hyperactivity rating scales did not differ between the two groups. There are several

mechanisms that could account for these discrepancies between our result and those two studies. In general these two studies use Conners' Rating Scale for teachers and parents so different informants identify different children as problematic; this is may be due to informant variance or instrument variance and sampling variance. On the other hand, differences in rate may stem from differences in the way each informants views the child, for instances, parent may deny the problem that are in fact present in the child perhaps out of a desire to see the child as healthy or normal, alternatively the parent may recognize the child's difficulty but attribute minimal negative consequence to it. Lastly different informants have different levels of exposure to the symptoms of problem behavior. In 6-12 years, the teacher's had direct information about the child performance in this context where as the parent must rely on proxy information from the child and teacher, presumably parents may often lack exposure to a comparison group and thus may fail to recognize that the child behavior is abnormal.

Regarding sport practice: Our results showed that BPD children were significantly participated, spent time and skilled in sport practice compared with ADHD children. This finding was supported by Tillman, *et al.,* (2001), who reported that children with BPD participated more in sport activity as a part from their disorder, (increase activity and increase in intensity in goal-directed activities related to social behavior). Also, Ward and Purvis, (2001), found that BPD child participated in sport more than child with ADHD, because child with ADHD has difficulty in following rules, has a short attention span, often fails to give close attention to details and difficulty in sustaining attention and while waiting in line, he will frequently kick or push the child next to him, always looking to move on to something new, action before thought. In contrast to our findings, DePauw, *et al,* (2000), reported that there was no significant difference between children with BPD and ADHD in sport participation. They explained their finding that families of children with BPD and ADHD always aware about precautions need to be taken to ensure safety for the children. These precautions would include the environment (field, court, etc.,), equipment, and knowledge of the rules. Our results revealed insignificant difference between children with BPD and children with ADHD in joining sport club. That could be explained by joining sport club controlled by several factors, like social class of the family. In Ismailia community most of the families have low to moderate socioeconomic resources, furthermore, the number of the sport club in Ismailia is few. In addition, there are no much differences between rural and urban areas. Also, most of the families are not interested in joining clubs due to their children disorders.

Regarding hobbies: It was shown that there was significant difference between BPD group and ADHD group in the presence of hobbies. This could be explained by inattention, poor concentration, and abrupt shifts in activity, lack of organization in ADHD children. This result is in agreement of Papolos and Papolos, (2002), and Krasa and Tolbert, (2003).

Regarding participation in house chores: It was found that there was insignificant difference between BPD children and ADHD children. That was inconsistent with the results of EL-Defrawi, *et al.*, (1997),

who found that child with psychiatric disorder do not share their family in house chores, because limitation in the child performance makes the child more dependent on the parents. Our results can be explained that in our study we have 45 female and in our culture the family was always aware about training girls on the housework to prepare girls to be a housewife.

Regarding social relationship: BPD group was significantly more socially comptent than ADHD group. A lesser, but still significant, difference was observed between BPD children and ADHD children in relationship with their parents. Our result was supported by the results of Seif-El-Din, *et. el.,* (2001), who found that the relationship with parents getting worse in about 63% of ADHD children and also, with the results of. Aziz (2002), who found that 35% of the BPD children had a bad relationship between their parents especially mothers especially during episode of the disorder, and 65% of the BPD children show a good relation with their parents or the same relation after or before the episode. Furthermore, our result agreed with Hans, (2002), who reported that the degree of social functional deterioration among BPD children is not as severe as that seen in ADHD children. This can be explained by the nature of the disorder; the disruptive behavior, moodiness, difficulty sleeping at night, impulsiveness, overactivity and inability to concentrate. All these have been associated with great familial loading (El-Batrawy, *et al.,* 2004). Also, the table showed that the relationship with siblings of the ADHD children was statistically significant worse than BPD children. This result was consistent with the results of Abdel-Gadir, *et.al.,* (2001), who found that (45%) of children with ADHD had a worse relationship with their siblings. Also, Lewine and his coworkers 2002 found that ADHD children show poor social adjustment, than BPD children. On the other hand, we found that BPD children had also a worse relationship with their siblings. Our findings was supported by Aziz, (2002), who found that 25% of the BPD children had a bad relationship between their siblings especially during episode of the disorder, and 75% of the BPD children show a good relation with their siblings or the same relation after or before the episode. This relationship can be explained on the base that these emotional and social difficulties in both groups and the illness leads to poor self image, decrease self esteem, decrease self confidence, social embarrassment and social restriction.

Regarding social activities: BPD children were more sociable than children with ADHD, as they had significant more number of friends, Also there were more socially involved with their friends within the last 6 months. Our results was supported by Akiskal and his coworkers 2000, who found that these children with early onset BPD had relatively good peer relationships. DeLong and Aldershof, (2000), reported that one-third (33.3%) were noted to posses leadership qualities; 68% of these children with early onset BPD were involved in a variety of extra-curricular activities and were seen by their teachers as making a positive contribution to their social life. This could be explained by the nature of the disorder which makes the child shows increase in goal-directed activity especially in school and excessive involvement in pleasurable activities. A markedly different peer relationship profile was shown in children with ADHD where two thirds of the chidren with ADHD were

described as having significant poor peer relationship and diminished extracurricular activities (El-Batrawy, *et al.,* 2004).

Regarding school performance: Our results revealed that poor school performance was found in both BPD group and ADHD group without significant difference that could be attributed primary to adjustment problems, the effects of multiple hospitalization and difficulties with peers (Salzman and Salzman, 2000). Also, cognitive deficits associated with BPD cause academic difficulties (Katcher, *et al.,* 1999; Riley, *et al.,* 2001). Additionally, the disorder itself may impede both cognitive and social functioning, leading to decreased academic ability. It is possible to hypothesize that disturbance in frontal lobe and/ or right hemisphere functioning in BPD children may, at least in part, be responsible for this finding (Burder, *et al.,* 2002). As regard, ADHD group, our finding was supported by Biederman, *et al.,* (2002), who found that the frequency of learning disabilities in ADHD ranged from 25% to 45%. Poor academic performance in ADHD could be regard as secondary to impairments of attention and behavior control. In addition, Sliver, *et al*., (2000), found that academic learning may also be impaired in children who have not developed. In the current study, BPD group showed a higher rate of arithmetic failure than ADHD group, that is consistent with the results of other previous studies that reported specific academic difficulties in children with early onset BPD specially problems in mathematics (Jamison, 2002; Menon, *et al.,* 2002). Arithmetic deficits could be due to underlying deficiencies in a number of cognitive processes, including retrieval of arithmetic facts from semantic memory, execution of arithmetical procedures, or visuospatial representation (Jamison, 2002). Functional imaging studies have demonstrated that mathematical reasoning involves a distributed network, including the lateral and ventral lateral prefrontal cortex and the posterior parietal lobe, as well as subcortical regions such as the caudate nucleus and cerebellum. Also, Specific deficits in mathematic were correlated with abnormalities in brain structure. For example, mathematics deficits in children with velocardiofacial syndrome have been related to structural abnormalities in the parietal lobe region (Menon, *et al.,* 2002). In the present study it was found that ADHD children showed a higher rate of failure in Arabic reading than BPD children that is supported by Rutter *et al*., (2001), who reported that student with reading disorder had an elevated rate of hyperactivity and inattention. Generally, we found that both BPD and ADHD children reported less than average level in academic performance this may be due to their illness. There is evidence from a number of studies which suggest that children with psychiatric disorder are underachiever and do more poorly in academically than do their healthy peers. Also, this can be explained by that children with psychiatric illness miss days of school because of acute exacerbation of their conditions, out patient health care related appointment, or hospitalization.

Regarding results of Child Behavior Checklist: We found that there was significant difference between BPD group and ADHD group in Internalizing and Externalizing problems as reported by parents. This result was consistent with the results of Dienes, *et al*., (2002), who found that children with BPD received elevated scores on the CBCL scales in comparison with non-clinical populations. In addition,

the BPD group differed from the ADHD group only on the aggressive behaviors, withdrawn and anxious/ depressed subscales of the CBCL. Hazell and Lewin, (2000), reported that BPD children may be distinguished from those with ADHD by the internalizing and externalizing symptoms in CBCL. Our results are inconsistent with the results of Chang, *et al.,* (2000), who found no significant difference between BPD children and ADHD in CBCL.

Regarding predictors of bipolar disorder in children: Multiple regression analysis revealed that the CARS for Mania was the most predictor tool for BPD in children than the YMR Scale-Parent Version, Conner Scale or CBCL. This result is consistent with the results of Alessia, *et al.,* (2002), who found that the CARS for Mania is a good tool to use in discriminate between ADHD and BPD. However, Pavuluri, (2002), explained that why the CARS for Mania is a good predictor for BPD. First: CARS is a shorter instrument than CBCL. Second: it is more specific in it's items than the conner´s scale. Third: the classification in CARS need only one scale, whereas the CBCL analyses use nine syndrome scale (externalizing and internalizing problems). Also, we found that the frequency of social involvement was a good predictor for BPD in children which was supported by other previous studies (Akiskal, *et al.,* 2000; DeLong and Aldershof, 2000), that could be explained by the nature of the disorder which makes the child shows increase the goal-directed activity and excessive involvement in pleasurable activities.

In Summary, 37.5% of children with ADHD met the criteria of bipolar disorder. A child with bipolar disorder can be misdiagnosed with ADHD because both BPD and ADHD share symptom characteristics of inattention, behavioral and emotional problems, impulsivity and even hyperactivity. Children with BPD have impairment in their social competencies, and have high level of behavioral difficulties. They also have learning difficulties; hence they are prone to school failure and poor academic performance. We are in agreement with many recent studies (Adler, *et al.,* 2005; Faraone, *et al.,* 2005; Kowatch, *et al.,* 2005; Udal and Groholt, 2006), to conclude that Child BPD severely impairs a child developmental and emotional growth. It is frequently misdiagnosed, resulting in inadequate management that worsening of the disorder. BPD is not often recognized in children and the child reports a long history of related psychopathology misdiagnosed as ADHD. Therefore the first and most important step in treating these children is accurately recognizing the disorder.

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